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ORGANIC CHEMISTRY

INCLUDING CERTAIN PORTIONS OF

PHYSICAL CHEMISTRY

FOR

MEDICAL, PHARMACEUTICAL, AND BIOLOGICAL STUDENTS

(WITH PRACTICAL EXERCISES)

BY

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PREFACE.

AMONG the most important of the recent advances in medical science are those relating to the chemistry of the various organic substances which enter into the composition of animal tissues and fluids, and to the physico-chemical laws which govern, or at least influence, many physiological processes. The discovery of the chemical constitution of the purin bodies, of many of the urinary constituents, and of sugars and fats, as well as the new theories of solution and catalysis, has revolutionized the teaching of biological and clinical chemistry; and in pharmacology and pharmacy a knowledge of organic and physical chemistry is almost essential. The study of these parts of chemistry is, therefore, daily coming to be of greater importance to the medical student and is already included in the curriculum of the best medical schools.[1]

As taught in the regular college classes in organic chemistry, the subject certainly absorbs too great a

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[1] The recent application by Arrhenius of certain physico-chemical laws in explaining the mode of action of antitoxins, etc., is an illustration of the increasing importance of a knowledge of physical chemistry for the medical student.

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ORGANIC CHEMISTRY.

CHAPTER I.

THE NATURE AND COMPOSITION OF ORGANIC COMPOUNDS.

Definition of Organic Chemistry. The various inorganic chemical compounds are classified by the chemist into groups, a group comprising all the compounds of some particular element. Thus we have the iron group, the sulphur group, and so on. On account, however, of the great number[1] of compounds containing the element carbon, the group of carbon compounds is set apart for consideration as a special branch of chemistry. Organic chemistry is that branch: *it is the chemistry of carbon compounds*. This definition is, however, not strictly accurate, for it is customary to treat of the oxides of carbon and the carbonates in inorganic chemistry.

The name organic owes its origin to the old-time belief that these compounds of carbon could be produced only by the agency of vegetable or animal organisms, by so-called vital activity. That such a notion is untenable was first shown by Wöhler, who, in 1828, obtained urea—the main organic constituent of urine—by simply evaporating an aqueous solution of ammonium cyanate, his real intent being to recrystallize the latter salt. Since that date thousands of organic compounds have been prepared in the laboratory without any assistance from vital processes. In fact, a great proportion of the compounds known to organic chemists have never been discovered in nature, but have been created in the chemical laboratory.

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[1] Over 100,000.

Elements and their Detection. In organic compounds carbon may exist in combination with one, two, three, four, or even five other elements. The most important elements present in organic compounds, together with their atomic weights and valences, are as follows:

Carbon, C.........	atomic	wt.	12,	valence	IV.
Hydrogen, H......	"	"	1,	"	I.
Oxygen, O........	"	"	16,	"	II.
Nitrogen, N.......	"	"	14,	"	III and V.
Phosphorus, P.....	"	"	31,	"	III and V.
Sulphur, S........	"	"	32,	"	II and VI.

Some important compounds contain the halogens (Cl, Br, I). The presence of most of these elements in organic compounds can be quite readily detected by simple tests, the principal ones being incorporated in the experiments that follow. The presence of oxygen cannot be directly determined.

Experiments. Detection of carbon, hydrogen, nitrogen, sulphur, and phosphorus.

(1) **C** and **H**. Dry a clean test-tube in the gas-flame.

Fit it with a cork through which passes a glass tube bent at a right angle. Mix in a mortar a little dry cane sugar and ten times as much dry CuO, pour this mixture into the test-tube, cork, and dip the outside end of the glass tube into baryta solution contained in another test-tube. Heat the sugar mixture over a flame. Drops of water condense on the cool parts, showing the presence of H. Cloudiness in the baryta is due to carbon dioxide, forming $BaCO_3$, and indicates the presence of C. By heating CuO it is reduced; its oxygen combines with the C and H of the organic substance to produce CO_2 and H_2O.

(2) **N** and **S.** (*a*) Triturate some dry albumin with twenty times as much soda-lime,[1] transfer the mixture to a test-tube, and heat over a flame. Test the vapour that appears for ammonia, the presence of which proves the existence of N in the compound examined.

(*b*) Put into a dried test-tube some dry albumin equal in bulk to a bean. Add a small piece of clean metallic sodium. Heat until the mass is red-hot, then *gently* drop the test-tube into a small beaker containing 10 c.c. of distilled water. The tube breaks, and NaCN and Na_2S go into solution. Filter and divide the filtrate into portions *A, B, C*, and *D*. To *A* add NaOH until strongly alkaline, then a few drops of freshly made $FeSO_4$ solution[2] and a drop of Fe_2Cl_6 solution. Boil this mixture two minutes, cool, and acidify with HCl. The appearance of a greenish-blue colour or a precipitate of Prussian blue indicates N. To *B* add a few drops of a *fresh* solution of sodium nitroprusside;[1] a reddish-violet colour points to the presence of S. To *C* add lead acetate solution and acidify with acetic acid. A brownish-black discoloration or precipitate is due to S. Neutralize *D* with HCl; add a few drops of Fe_2Cl_6 solution: a red colour, which is removed by $HgCl_2$, is caused by the presence of sulphocyanide.

---

[1] Soda-lime is made by placing a saturated solution of caustic soda in a porcelain basin and gradually adding powdered quicklime to it, with constant stirring, until the contents become solid, forming small lumps.

[2] Sodium ferrocyanide is formed by this treatment.

If sulphocyanide is not formed in examining an organic compound by this method, halogens may be tested for in the filtrate by boiling some of it with HNO_3 (HCN or H_2S driven off) and then testing with $AgNO_3$ (precipitate of AgCl, AgBr, or AgI).

If it is desired to detect N, S, or halogens in a liquid it is best to drop the liquid on to melted sodium contained in a test-tube which is held vertically by being thrust through a hole in an asbestos pad.

(3) **P.** Mix some dry nucleoproteid (or dry yeast) with twenty parts of fusion mixture (1 part $Na_2CO_3 + 2$ parts KNO_3). Heat in a crucible until the mass becomes white. When cool, dissolve it in a little hot water and pour the resulting solution into an evaporating dish. Add HCl until neutral and filter. To half of the filtrate add NH_4OH until strongly alkaline, then add magnesia mixture.[2] The phosphates, formed by the oxidation of the phosphorus of the compound, cause

---

[1] Formula = $Na_2Fe(CN)_6(NO)$.

[2] Magnesia mixture is made as follows: Dissolve 55 gm. of pure $MgCl_2$ crystals and 70 gm. NH_4Cl in 1300 c.c. of water and add 350 c.c. of 8% ammonium hydroxide.

a white precipitate. To the other half of the filtrate add HNO_3 until strongly acid, then add an equal volume of ammonium molybdate solution[1] and heat in a water bath until a *fine* yellow precipitate appears.

Having thus determined what elements are present in the organic compound that he is investigating, the chemist next proceeds to its more thorough examination. He first estimates the percentage amounts of the various elements contained in the substance, and then he determines its molecular weight. He is able from these data to calculate the empirical[2] formula. But more than one substance may have this same formula; therefore he studies the reactions of the compound when treated with reagents in order to get a clue as to how its molecule is built up, that is, how its atoms are linked together. And, finally, by causing simpler substances, the structure of whose molecules is known, to become united (*synthesis*), he endeavours to produce a substance having the same molecular structure as his compound. If his synthetic compound shows properties that are identical with the substance under examination, the chemist then considers that he has established with absolute certainty the chemical construction of the compound.

But all this work will end in failure unless the substance under examination be absolutely pure, i.e., free from admixture of any other substances. It is necessary for us at this stage, therefore, to explain the chief methods of purification as well as the tests by which the purity of the substance is ascertained. This will be done in the chapter that follows.

---

[1] Ammonium molybdate solution is made as follows: Dissolve 75 gm. ammonium molybdate in 500 c.c. of water and add 500 c.c. of HNO_3 of specific gravity 1.2.

[2] The empirical formula gives merely the total number of atoms of each element in one molecule, as $C_6H_{12}O_6$ (see p. 57).

CHAPTER II.

PURIFICATION AND IDENTIFICATION OF SUBSTANCES.

PURIFICATION OF SUBSTANCES.

THE main methods of separating an organic substance in a pure state are *crystallization*, *sublimation*, *distillation*, and *dialysis*.

Crystallization. The basis of this method is the fact that different substances are not usually soluble to an equal extent in the same solvent. For example, acetanilide can be separated from dextrose by dissolving the mixture of these two in hot water: on cooling the resulting solution, the acetanilide crystallizes out because of its slight solubility in cold water, while the dextrose remains in solution. By repeated crystallization in this manner perfectly pure acetanilide can be obtained (see exp. below).

Inasmuch as crystallization as a method for separation and purification of organic compounds is invaluable, it will be well to detail specific directions for carrying it out. (1) Carefully select a suitable solvent. Put small quantities of the substance to be purified into several test-tubes; add to each a different solvent—those most commonly used are water, alcohol, ether, chloroform, benzol, petroleum ether, acetone, and glacial acetic acid. Discard those which dissolve the substance readily. Heat each of those that remain. Choose the solvent which when hot dissolves the substance readily, but deposits crystals on cooling. The solvent should either hold the impurity in solution when cold or else exert no solvent action on it whatever.

(2) Completely saturate at boiling temperature a certain quantity of the chosen solvent with the substance.

(3) Filter the hot liquid through a plaited filter, using a funnel with a short stem. (With a long-stemmed funnel crystals may separate out in the stem and block it.) Heating the funnel in hot water before filtration may be resorted to.

(4) Collect the filtrate in a beaker having a capacity twice the volume of the liquid. With too small a beaker creeping of crystals and liquid over the edge may occur.

(5) Cool slowly. If crystals are deposited very quickly, redissolve with the aid of heat, and prevent rapid cooling by wrapping the beaker with a warm towel.

(6) Cover the beaker with a piece of filter-paper to prevent condensation-drops falling back into the liquid and disturbing the crystallization. A watch-glass or glass plate completes the covering.

(7) Do not disturb the beaker until crystals have formed. If their appearance is greatly delayed they may often be induced to form by scratching the inner wall of the beaker with a glass rod, or by "sowing" a crystal of the substance into the liquid.

(8) If the substance is not sufficiently insoluble in the cold solvent, crystallization may be brought about by slow evaporation in a wide crystallization dish which is loosely covered.

(9) Collect the crystals on a suction-filter; wash them with a little of the pure cold solvent. Reject the crystals that have crept above the surface of the liquid.

(10) Dry the crystals in a desiccator, except when they contain water of crystallization.

EXPERIMENT. Put 20 c.c. of distilled water into a beaker and heat to boiling on an asbestos pad. Completely saturate it with the mixture of dextrose and acetanilide which is furnished. Filter while hot, and cool. When a good crop of crystals has formed, separate them by filtration. Dissolve and recrystallize. Repeat the process until the filtrate from the crystals no longer reduces Fehling's solution.[1] At least three crystallizations should be carried through. Save the pure white crystals. After drying them in a desiccator a determination of their melting-point may be made (see below).

To test the purity of the crystals their melting-point is determined. The method of making a melting-point determination will be described in the experiments that follow. Pure crystals melt quite sharply and completely, i.e., they become completely melted within 0.5° C. The crystals may be considered pure when, after repeated crystallization, the melting-point remains constant for several successive determinations. A bath of water may be used for substances having a low melting-point (as below 80°[1]). Sulphuric acid is used for higher temperatures (up to 280°). For still higher temperatures paraffin is used.

---

[1] Fehling's reagent consists of an alkaline solution of cupric hydroxide, the latter being held in solution by means of Rochelle salt. The reagent is of a deep-blue colour, and when it is boiled with even a trace of dextrose a red precipitate forms in it.

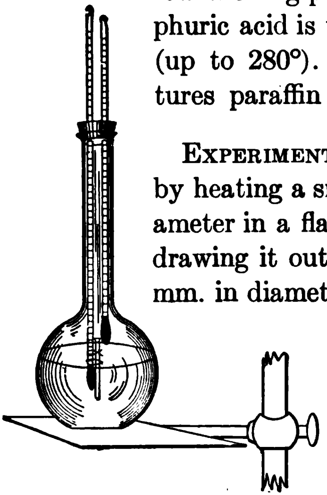

FIG. 1.

EXPERIMENT. Make melting-point tubes by heating a small glass tube of 4 mm. diameter in a flame until red, then suddenly drawing it out. A capillary tube about 1 mm. in diameter is thus obtained. Break into lengths of 6–8 cm. and seal one end of each. Put into such a tube some powdered chloral hydrate which has been dried in a desiccator. Attach the tube to a thermometer by means of a narrow rubber band cut off from rubber tubing, adjusting it so that the main part of the chloral will be opposite the middle of the bulb of the thermometer. Suspend the thermometer in a beaker of water so that the bulb is fully immersed. Heat the water very gradually. Note the temperature at which there is the first indication of melting, also the temperature of actual fusion.

Into another capillary tube put pure dried powdered urea;[1] attach the tube to a thermometer with a fine platinum wire, adjusting it as above. The bath in this case should be pure H_2SO_4 almost saturated with K_2SO_4 (to lessen fuming), contained in a long-necked Jena flask (as, for example, a Kjeldahl incineration-flask). By means of a loosely fitting cork suspend the thermometer in the flask, with its bulb dipping into the bath. In a similar manner suspend another thermometer to take the temperature of the air above the H_2SO_4. Heat gradually. When melting occurs, place the bulb of the second thermometer midway between the meniscus of the mercury in the stem of the first thermometer and the surface of the bath; from this quickly make the reading of the air temperature (this is t in the formula below). Also measure in degrees the height of the mercury column above the surface of the H_2SO_4 ($=L$ in the formula). *The correction which must be added* to the observed reading (which is T) on account of the stem of the thermometer and mercury thread being cooler than the bulb can be calculated by the formula: $L(T-t)(0.000154)$. The corrected[2] melting-point of pure urea is 132.6°.

---

[1] All temperatures given in this book are centigrade.

A method of purification applicable to certain solid substances is **sublimation.** A substance sublimes when it passes from the solid state to a vapour without melting. The method is carried out as follows. A watch-glass or evaporating dish containing the substance is covered with filter-paper which has several pin-hole perforations. A funnel which is of a size to fit neatly is inverted over this, the stem being loosely plugged with cotton. The dish is heated gradually until vapour passes into the upper chamber of the apparatus and condenses on the cool walls of the funnel (see exp., p. 276).

---

[1] Where "pure urea" is called for it is best to prepare it by recrystallizing some urea from hot absolute alcohol.

[2] The melting-points marked "corrected" are quoted from *H. Meyer's* Analyse und Konstitution der organischen Verbindungen.

Distillation. This method is useful mainly for the purification of liquids. Certain solid substances, however, can be distilled to advantage. When the impurity is a material that will not vaporize at the temperature employed (i.e., at a temperature at which the substance itself readily vaporizes), simple distillation suffices. When, however, a mixture of volatilizable liquids is dealt with, fractional distillation has to be resorted to. This method is described in the following experiment. Certain mixtures cannot be resolved into their constituents in the pure state by fractional distillation, such as a mixture of water and alcohol, or methyl alcohol and benzol.

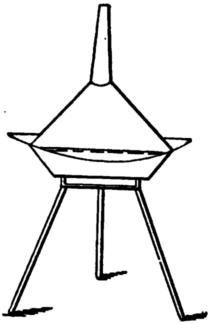
FIG. 2.

EXPERIMENT. Set up a distillation apparatus as shown in the diagram. Into the fractionating flask—a flask having a branch tube fused into the neck as a delivery-tube for the vapour—pour through a funnel about 300 c.c. of 50% alcohol. Select a cork that will fit the flask tightly. Through a hole in the cork insert a thermometer, and hang it so that the bulb is in the stream of vapour, i.e., opposite or below the opening of the side tube. The bulb must not be below the neck nor low enough to be splashed by the boiling liquid. Heat gradually on a water bath. Have four clean receiving flasks ready and labelled. In the first flask collect all the distillate coming over while the thermometer registers a temperature between 78° and 83°; in the second flask collect that distilling between 83° and 88°. Now dry the outside of the fractionating flask with a cloth and change it to a sand bath. Flask number three is to catch the distillate between 88° and 93°. The last flask receives all that distils over above 93°.

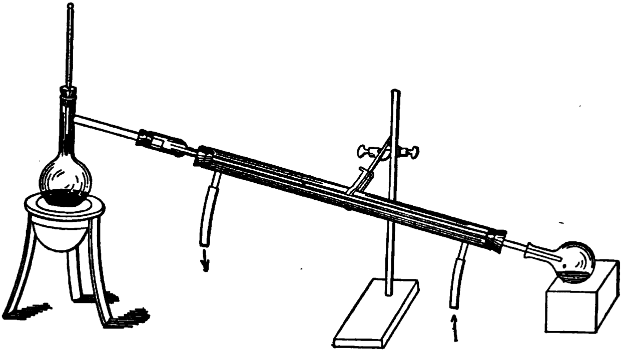

FIG. 3.

For the second distillation use a smaller fractionating flask or a flask with a bulbed column attached as shown in the diagram. Pour into it the fluid in flask number one and use the latter as the first receiving flask for the distillate. When the temperature reaches 83° pour the contents of flask number two into the fractionating flask, and when the temperature again rises to 83° replace flask number one by flask number two as the receiver. When the temperature reaches 88° add the liquid in flask number three to the fractionating flask, and continue in like manner as directed above until all the "fractions" of the first distillation have been redistilled. If time permits, carry through a third fractional distillation. By repeated fractionating practically all of the alcohol is brought into flask number one and most of the water into flask number four. Save the final first fraction and later determine the per cent of alcohol by taking the specific gravity (see p. 18) and comparing with the table (see p. 345).

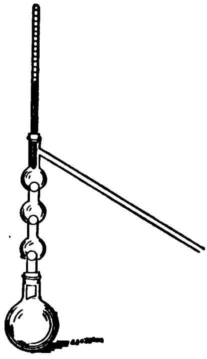

FIG. 4.

Distillation is sometimes carried out by bubbling steam through the mixture, which is kept at a temperature of at least 100°. By this means substances which boil even above 200° can be obtained in the distillate, mixed, of course, with a large quantity of water (see fig. 5).

Vacuum distillation is employed in certain cases, particularly when it is desirable to lower the boiling-point in order to prevent any decomposition of the substance. Many substances decompose at a temperature below their boiling-points. The distilling apparatus is closed up air-tight except for a finely pointed tube which dips below the surface of the heated liquid and, passing through the stopper, is open to the air:

through this tube fine bubbles of air keep the contents of the flask in commotion and prevent bumping. The receiving flask is connected with a suction-pump. A reduction of pressure in the apparatus to 30 mm. of mercury (atmospheric pressure being about 760 mm.) will usually lower the boiling-point of a high-boiling substance by nearly 100°. An ordinary suction-pump is usually quite satisfactory for lowering the pressure (see fig. 6).

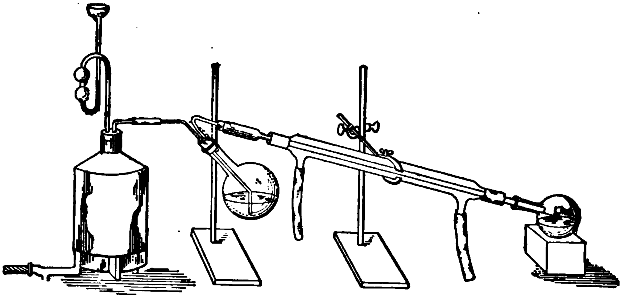

FIG. 5.

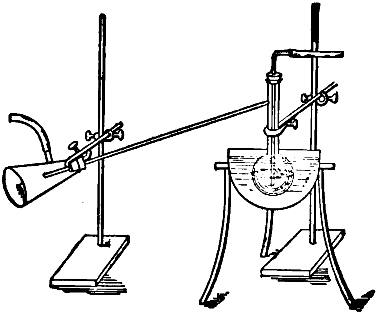

FIG. 6.

The test of purity of a substance that distils is constancy of boiling-point. If, after repeated fractional distillation, a material is obtained which has the same boiling-point each time and which distils over completely at that temperature, it is most likely a pure substance.

EXPERIMENT. The boiling-point flask should be either a long-necked fractionating flask which has the side tube coming off very high up near the cork, or an ordinary fractionating flask into whose neck is fitted an open tube slightly expanded at the lower end so as to fit the neck, while the latter has been dented with a blast-flame at the proper point to prevent the tube slipping into the chamber of the flask (see fig. 7). In such an apparatus the vapour passes up to the cork, then descends outside the tube, heating the stem of the thermometer for the whole length of the mercury column, the thermometer being lowered sufficiently to permit this.

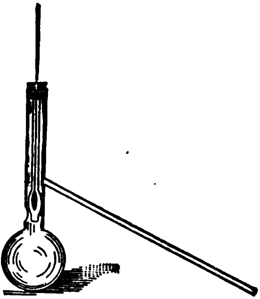

FIG. 7.

Put 20 c.c. of pure chloroform into the flask; support the flask on wire gauze (it is advisable to interpose between the gauze and the flask an asbestos pad having a hole 1–2 in. in diameter). Attach a long tube as an air-condenser and place a receiving flask in position. Heat with a small flame. When vapour passes freely into the condenser, note the temperature. Continue distillation until the temperature has remained constant for at least five minutes. Take the reading as the boiling-point. No correction is necessary except for barometric pressure. This correction can be calculated approximately by adding to the observed boiling-point 0.1° for each 2.7 mm. below 760 mm. barometric pressure or subtracting 0.1° for each 2.7 mm. above this. The boiling-point of chloroform at 760 mm. pressure is 61.2° (corrected).[1]

Dialysis is occasionally employed for purification purposes, especially in bio-chemistry. It depends on the well-known fact that crystalloids can diffuse through animal membranes or parchment paper, whereas colloids cannot. Thus, to separate sodium chloride from egg proteid a solution containing these is placed in a dialyser suspended in pure running water: the sodium chloride diffuses out, leaving the egg proteid in the dialyser.

IDENTIFICATION OF SUBSTANCES.

When the substance has been purified by the above methods, identification may be attempted. For this purpose its *physical properties* are studied; its colour, odour, and taste are carefully noted, and determinations are made of its melting-point, boiling-point, crystalline form,—including measurement of the angles of the crystals,—density or specific gravity, action on polarized light, spectroscopic appearance, refractive power, and solubilities. The data thus obtained are compared with those of known substances.

---

[1] The boiling-points marked "corrected" in this book are those given in *Traube's* Physico-chemical Methods.

Next to the first five properties mentioned, the most universally useful one for purposes of identification is specific gravity. The method of determining this we will describe here. Those of the other properties not already described will be found in one or another of the larger laboratory manuals.[1]

The specific gravity of liquids may be found by several different methods. 1. The weight of equal volumes of the liquid and of water may be successively determined in a special stoppered bottle called a *picnometer*. The temperature of both fluids at the moment of weighing must be reported. The temperature of the water taken as the standard for comparison may be 0°, 4°, or 15°. The most convenient form of picnometer is one which holds exactly 10, 25, or 50 gm. of pure boiled water at 15° (see fig. 8). Further details are explained in the experiment below.

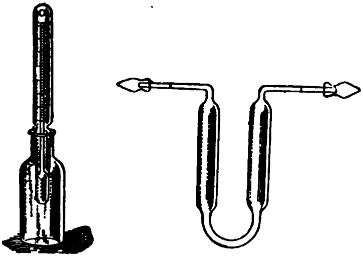

FIG. 8.

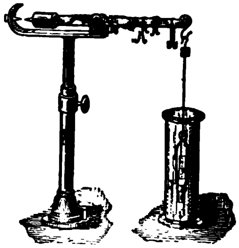

FIG. 9.

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[1] *Gattermann.* The Practical Methods of Organic Chemistry. Translated by Schober. 2d American edition.

Mulliken. Identification of Pure Organic Compounds.

Lassar-Cohn. Laboratory Manual of Organic Chemistry; also, Arbeitsmethoden für organisch-chemische Laboratorien. 3d edition (1903).

2. *Westphal's balance* is a very useful instrument for finding specific gravity (see fig. 9). Riders of different sizes are used on this balance, each one representing a different decimal place in the specific gravity. This instrument gives the specific gravity of the liquid at the temperature of observation compared with pure water at 15°.

3. The *hydrometer* is another empirically graduated instrument for determining specific gravity, water at 15° being the standard. It is a glass float having a long stem; this sinks in the fluid, so that the surface comes to a certain mark on the stem, and the figures which are read off at that mark indicate the specific gravity (see fig. 10).

The urinometer is a hydrometer for use with urine.

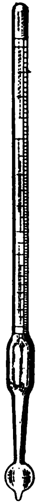

FIG. 10.

The specific gravity of a solid can be found by weighing it in the air, then reweighing it while immersed in water. This method has very little application in organic chemistry. The specific gravity of crystals or small solids can be determined by placing an accurately weighed quantity of them in a picnometer filled with some liquid in which they are insoluble (see exp. below).

EXPERIMENTS. (*a*) *Specific gravity of petroleum ether.* Weigh accurately an empty dry picnometer which will hold just 25 gm. of pure water at 15°; deduct from the weight 0.03 gm. for the weight of the contained air. Remove the stopper and fill with petroleum ether. Wrap a strip of folded filter-paper about the neck to catch the overflow, insert the stopper so that no air is left in the bottle, wipe off gently, and reweigh. When weighed, note the temperature as indicated by the thermometer in the stopper, also make sure that no air has been drawn into the bottle by cooling and consequent contraction of the fluid. The difference between the two weights gives the weight of the petroleum ether, and this divided by the weight of an equal amount of water (25 gm.) gives the specific gravity as compared with water at 15°. In recording specific gravity report the temperature of observation; for example, petroleum ether $S\frac{18^\circ}{15^\circ}=0.7$ means that the specific gravity of petroleum ether at 18° is 0.7 when compared with water at 15°.

(*b*) *Specific gravity of urea.* Weigh a little test-tube which contains pure dry urea crystals. Remove the stopper of the picnometer used in (*a*); pour the urea into the petroleum ether. Now fill the neck with more petroleum ether, insert the stopper as before, and reweigh. The petroleum ether must be at the same temperature as in (*a*). Reweigh the urea tube; by deducting this weight from the previous one find the weight of the urea in the picnometer. To find how much petroleum ether has been displaced by the urea (the latter being insoluble in the former) add to the weight of the bottle filled with petroleum ether (exp. *a*) the weight of the urea, then deduct from this sum the weight of the bottle containing urea immersed in petroleum ether (*b*); the difference is the weight of the petroleum ether displaced. Divide this by the specific gravity of petroleum ether; the result indicates the displacement in cubic centimetres, or rather the weight (in grams) of an equal quantity of water, so that the weight of the urea used divided by this figure gives the specific gravity. The specific gravity of urea is about 1.33.

If the substance under investigation is known to chemists it can generally be identified by comparing the data gathered as to its properties with tabulated lists[1] of boiling-points, melting-points, specific gravities, etc. Generally an accurate determination of the boiling- or melting-point and of the specific gravity will definitely locate the substance. When dealing with a liquid it is advisable, if there exists any doubt about the nature of the substance, to determine the specific gravity at several different temperatures.

If the substance is still unknown or cannot be positively identified, an accurate analysis is made to determine the percentage by weight of each element present in it.

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[1] Such tables may be found in Physikalisch-chemische Tabellen by *Landolt and Börnstein* (1905 edition), Chemiker-Kalendar by *Biedermann* (yearly editions), Melting and Boiling Point Tables by *Carnelly* (1885).

CHAPTER III.

ELEMENTARY ANALYSIS.

The estimation of the carbon and hydrogen present in a compound is made by combustion in the presence of cupric oxide, the end-products of combustion being carbon dioxide and water. The method is in principle exactly the same as that for the detection of carbon and hydrogen.

The combustion is carried out in a glass tube of difficultly fusible glass having an inside diameter of about 1.5 cm. This tube should be 10 cm. longer than the furnace in which it is to be heated—85 cm. is a good length. A tube of this length is charged for combustion as follows: a short roll or spiral of copper gauze is inserted and pushed in 5 cm. from the end, moderately coarse cupric oxide (of wire form) is poured into the other end until it occupies 35–40 cm. of the tube next to the spiral, then another short copper spiral is pushed down to the coarse oxide to hold the latter in place, the next 20 cm. of the tube is occupied by the substance to be analyzed mixed[1] intimately with fine cupric oxide

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[1] The substance may be placed in a little platinum or porcelain boat instead of being mixed with CuO. If a liquid is to be analyzed it is sealed in a little glass bulb, and this is placed in the combustion-tube.

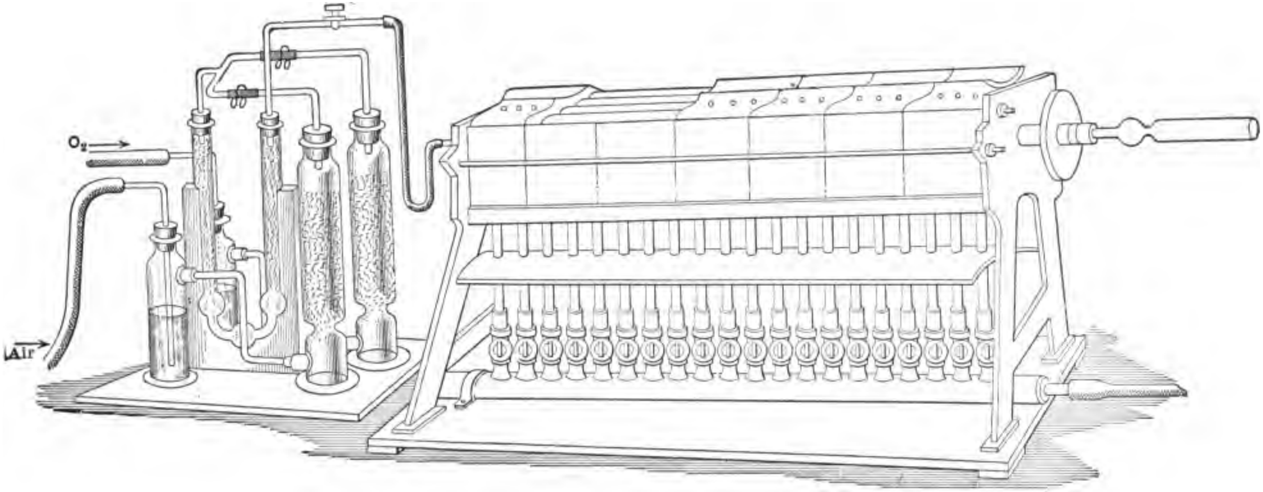

FIG. 11.

(wire form) in the manner described in the experiment below, then follows a short copper spiral (which has a wire loop attached) and finally some coarse cupric oxide. Each end of the tube is closed with a rubber stopper. Through the stopper at the end nearest the fine oxide mixture passes a glass tube which is connected with the apparatus for purifying the incoming air or oxygen.

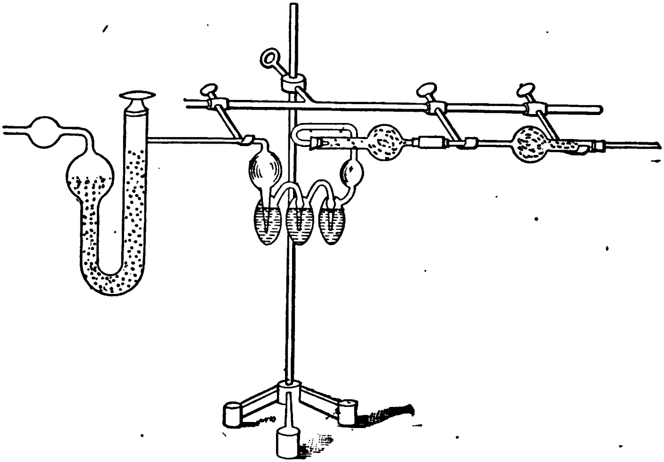

FIG. 12.

The absorption apparatus which collects the products of combustion is connected directly with a glass tube passing through the stopper at the other end.

When a tube is in service for the first time, to insure complete removal of any organic matter that might be clinging to the glass or the copper oxide, the fine oxide is used unmixed with any other substance, and the whole tube is heated for several hours while a stream of dry air is passing through. In this case an ordinary calcium chloride tube takes the place of the absorption apparatus. If moisture has collected in the tube toward the end it must be removed by warming the tube at that point. A stream of air can be used for the combustion process. Pure oxygen, however, is very much better for substances that do not oxidize readily, because of the rapidity and completeness of combustion in its presence. With oxygen completion of the process is indicated when the outgoing stream from the absorption apparatus causes an ember on the end of a splinter of wood to glow brightly.

It may add to the understanding of the process to trace the air or oxygen stream through the whole apparatus (see fig. 11). It first bubbles through a strong solution of caustic potash, which removes most of the carbon dioxide; then passes through a large U-tube or drying-tower containing soda-lime or small pieces of NaOH, which removes the last traces of carbon dioxide; then through another U-tube containing calcium chloride, which removes moisture.[1] The dry gas passes into the combustion-tube; when it reaches the fine copper oxide it aids the oxidation of the organic substances, and carries along with it the carbon dioxide and steam produced, also any volatilized material which has not been oxidized, and brings them into contact with the coarse copper oxide, which completes the oxidation; thus the stream when it reaches the end of the tube consists of air or oxygen containing carbon dioxide and water-vapour. In passing through the calcium chloride tube of the absorption apparatus the water is absorbed, and finally in bubbling through the caustic potash solution of the absorption bulbs the carbon dioxide is removed; the slight amount of moisture picked up here is removed by the straight calcium chloride tube (see fig. 12). The details of the method are given in the following experiment.

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[1] To insure thorough drying the air is sometimes finally bubbled through sulphuric acid.

FIG. 13.

EXPERIMENT. *Combustion analysis of salicylic acid.* The combustion-tube has been charged and thoroughly heated as directed above. Remove the stopper at the end nearest the air-tank, quickly pour out the coarse oxide into a clean dry beaker, pull out the short spiral, finally pour out the fine oxide into another beaker and replace the stopper. Put the beakers and the spiral into a desiccator. Weigh accurately a weighing-bottle containing about 0.2 gm. of pure salicylic acid which has stood in a desiccator several days. Through a clean short-stemmed funnel pour the salicylic acid into the mixing-tube (see fig. 13); add some of the fine oxide carefully through the funnel in such a way that all the crystals of salicylic acid are carried along with the CuO into the mixing-tube. When the tube is half full, insert the stopper; hold the tube and stopper firmly and shake very vigorously. When well mixed, quickly empty the contents into the combustion-tube; rinse the mixing-tube by shaking successively with small portions of fine oxide until all the oxide has been transferred to the combustion-tube. Replace the spiral and pour in the coarse oxide. Replace the stopper and connect with the air-purifying apparatus and start the air stream. The $CaCl_2$ tube remains at the other end of the tube. Reweigh the weighing-bottle.

Begin lighting the burners at the end near the calcium chloride tube. Start one burner at a time and with the lowest flame possible, then very gradually increase the flames in number and size. Do not heat the fine oxide at all. In the meantime weigh the calcium chloride absorption-tube and the caustic potash bulb with its calcium chloride tube (remove the plugs before weighing). When the coarse oxide has been brought to a dull red heat, the part of the tube which contains this having been covered with tiles, attach the absorption apparatus in place of the ordinary calcium chloride tube. Now start the heating of the other end of the tube, containing the fine oxide and the substance, very gradually. When the fine oxide is heated watch closely, and turn down the burners here if bubbles pass too rapidly through the potash bulbs. The bubbles should not go so fast that they cannot be easily counted. Finally, bring the whole tube to a dull red heat (never hotter). After thirty minutes at this temperature begin to cool the tube by gradually turning down the burners from each end. Do not remove the tiles. During the first fifteen minutes of cooling pass the air stream more rapidly to sweep out of the tube all water-vapour and carbon dioxide. Disconnect the absorption tubes, put on the plugs, and allow to cool. When cool, reweigh after removing the plugs. Do not forget to attach the calcium chloride tube in the place of the absorption apparatus. Before the combustion-tube is used for another analysis it should be heated for an hour while dry air is passed through it.

The increase in weight of the U calcium chloride tube indicates the weight of the water produced by the combustion. One ninth of this is hydrogen, therefore the per cent of hydrogen present in the substance burned can be obtained by the following formula:

$$\text{Per cent H} = \frac{\text{wt. of } H_2O \text{ produced} \times 100}{9 \times \text{wt. of substance burned}}.$$

The increase in weight of the potash bulb and straight calcium chloride tube is equal to the weight of the carbon dioxide produced. Carbon represents $\frac{3}{11}$ of this, therefore for calculating the per cent of carbon the formula used is:

$$\text{Per cent C} = \frac{\text{wt. of } CO_2 \text{ produced} \times 3 \times 100}{11 \times \text{wt. of substance burned}}.$$

The sum of the per cents of hydrogen and carbon deducted from 100 gives the per cent of oxygen.

If the substance contains *nitrogen*, oxides of nitrogen may be formed when the substance is oxidized as above. This necessitates a special modification of the method, because these oxides are absorbed by caustic potash. A long copper spiral (12–15 cm.), which has been reduced to pure copper by dipping it while hot into alcohol,[1] is put into the end of the tube nearest the weighed absorption apparatus, in the place of part of the coarse oxide. When the nitrogen oxides come in contact with the hot reduced copper they are deprived of their oxygen by the copper, and nitrogen is set free.

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[1] By this treatment any oxide adherent to the copper yields up its oxygen to oxidize the alcohol to aldehyde.

Of course a free stream of air or oxygen cannot be used in this case until combustion is complete, otherwise the reduced copper spiral would become oxidized and be rendered useless. The air stream is used to clear carbon dioxide out of the tube at the start before the heat is applied to the reduced copper spiral; during combustion the air is shut off; when combustion is complete the air stream is again turned on to remove all the products from the tube.

To estimate the nitrogen alone in an organic substance the same tube as that described above for nitrogenous substances can be employed, provided a stream of dried carbon dioxide gas, instead of air, is used for removing the gases, etc., produced by the combustion and for clearing out the nitrogen and oxygen contained in the tube before the heating is begun. The absorption apparatus in this case is a gas burette (a burette closed with a glass cock at the top) having some mercury in the bottom to act as a valve, and filled with a strong solution of caustic potash (see fig. 14). When bubbles

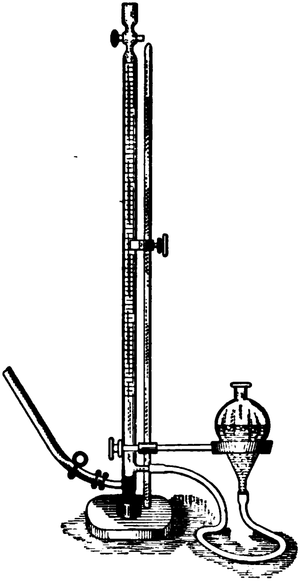

FIG. 14.

no longer collect at the top of the burette and the latter remains full of caustic (i.e., when only carbon dioxide is passing out of the tube), the carbon dioxide is shut off and combustion is carried out by heating the tube gradually up to a dull red heat. When combustion is completed carbon dioxide is passed again until the tube is cleared of nitrogen, as shown by the volume of the gas in the burette remaining constant. The caustic potash absorbs all the products of combustion except nitrogen. The burette is allowed to stand until the next day. The caustic potash in the reservoir is brought to the same level as that in the burette, and the number of cubic centimetres of gas is read off. The temperature of the nitrogen is found by placing a thermometer against the burette, with the bulb at the mid-level of the gas. Saturation with aqueous vapour may have been rendered certain by previously running in 1 c.c. of water carefully by way of the tap at the top.[1] The barometric reading must also be taken. The results of the analysis are then computed by referring to specially prepared tables which give in grams the amount of nitrogen corresponding to 1 c.c. of the moist gas in the burette, at various temperatures and under various pressures (see Appendix, p. 347).

An easier method of nitrogen estimation is the *Kjeldahl method*, by which the nitrogen in the organic substance is converted into ammonia by heating with pure sulphuric acid. The ammonium sulphate produced can then be treated with alkali, and the ammonia thus liberated distilled into a measured quantity of standard acid. From the amount of this latter which is thus neutralized, the amount of nitrogen contained in the organic substance can readily be calculated. Kjeldahl's method is extensively employed in biochemical analysis and will be found fully described in many of the laboratory manuals on that subject.

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[1] In doing this, of course, great care must be taken that no air enters the burette. The top of the burette being partly filled with water, the levelling-tube is then *slightly* lowered so as to cause a slight suction-pressure in the burette, and the tap is very cautiously opened and is closed as soon as the walls of the burette are moistened.

If halogens are present in the substance to be analyzed a silver spiral must be used in place of the reduced copper spiral. The silver combines with the halogens and prevents them passing into the absorption tubes, where they would be absorbed.

When sulphur is present lead chromate takes the place of the cupric oxide in the tube, lead sulphate being formed during combustion.

Having determined the percentage composition, a *provisional formula* for the compound may be found as follows: divide the percentage number of each element by its atomic weight, divide each of the resulting figures by the smallest of them (as the greatest common divisor), and make use of these smaller figures, or the nearest whole number, to express the number of atoms of each element in one molecule. An example will illustrate this. Alcohol was found by one analysis to contain 52.05% C, 13.13% H, and 34.82% O. Then

$$\begin{array}{lll}
\mathrm{C} & 52.05 \div 12 = 4.337; & 4.337 \div 2.176 = 1.993 \\
\mathrm{H} & 13.13 \div 1 = 13.130; & 13.130 \div 2.176 = 6.030 \\
\mathrm{O} & 34.82 \div 16 = 2.176; & 2.176 \div 2.176 = 1.000
\end{array}$$

Therefore the formula may be C_2H_6O. The same percentage composition would, however, be shown by any substance having the formula $C_{2n}H_{6n}O_n$. It becomes necessary then to determine the number of atoms in the molecule by finding out the molecular weight; the value of n is thus discovered.

CHAPTER IV.

MOLECULAR WEIGHT DETERMINATION. THE NATURE OF SOLUTIONS. OSMOTIC PRESSURE. IONIZATION. COLLOIDAL SOLUTIONS.

In order to understand fully the physico-chemical nature of solutions and the subject of molecular weight determinations it will be advisable briefly to review some of the cardinal points in physical chemistry which relate to these subjects. As we shall see later, gases and solutions in their physico-chemical behaviour are very much alike, so that a clear conception of the gas laws, which are well known and readily tested, will enable us to study more satisfactorily the nature of solutions.

The three important gas laws are as follows:

1. *Gay-Lussac's or Dalton's law:* provided its pressure remains unchanged, every gas expands by $\frac{1}{273}$ *of its volume at* 0° for each degree of rise of temperature.

Thus a gas occupying a volume of 1 litre at 0° will occupy 2 litres at 273°, if the pressure remains constant. In making calculations it should be remembered that the absolute temperature of 0° is 273°, and therefore for any temperature above 0° the absolute temperature is that temperature plus 273°. Another way of stating the law is that the volume of a gas (at constant pressure) varies directly with its absolute temperature.

2. *Boyle's law:* provided the temperature remains constant, the volume of a gas varies *inversely* as the pressure. Thus, if 1 litre of gas be compressed into the space of 0.5 litre, the pressure has been doubled.

3. *Avogadro's hypothesis:* under the same conditions of temperature and pressure, equal volumes of all gases contain the same number of molecules.

THE MOLECULAR WEIGHT OF GASES AND VAPOURS.

The relative weights of equal volumes of different gases, under the same conditions of temperature and pressure, must represent the relative weights of the molecules (Avogadro's hypothesis). If, then, we take the weight of one gas as the standard, the molecular weights of other gases can readily be ascertained. Hydrogen is the gas thus chosen, and since its molecule contains two atoms, we ascribe to it a molecular weight of 2. Similarly, oxygen has a molecular weight of 32, being sixteen times heavier than hydrogen. Two grams of hydrogen at 0° and 760 mm. Hg pressure has a volume of 22.4 litres. But 2 is the molecular weight of hydrogen; therefore if we take the number of grams of any other gas equivalent to its molecular weight this amount of gas will also occupy a volume of 22.4 litres (at 0° and 760 mm.). Such a weight in grams corresponding to the figures for the molecular weight is called a *gram-molecule* or a *mol.* In consequence of Boyle's law it must follow that if we compress a mol of any gas at 0° to the volume of 1 litre it will have a pressure of 22.4 atmospheres (i.e., 22.4×760 mm. Hg).

If, therefore, we know the volume, temperature, and pressure of a known weight of a gas it is easy by applying the above laws to determine its molecular weight. As an example, suppose that 0.2 gm. of a dry gas has a volume of 50 c.c. at 10° and 740 mm. Hg; what is the molecular weight?

$$50\times\frac{273}{273+10}\times\frac{740}{760}=46.899=\text{c.c. at }0^\circ\text{ and }760\text{ mm.}$$

But a mol occupies 22400 c.c. Then 0.2 gm. is $\frac{46.899}{22400}$ of a mol, therefore the mol is 95.4 gm. The molecular weight is 95.4.

Vapours obey the same laws as gases. Substances, solid or liquid, which can be vaporized by heat submit to a molecular weight determination as readily as gases. In practice the determination is made either by weighing a known volume of the substance in the form of vapour, or by measuring the volume of the vapour produced from a known weight of the substance.

A known volume of vapour is weighed when *Dumas' method* is used. By this method an indefinite quantity of the substance is vaporized in a flask-like bulb by heating the bulb in an oil-bath. The neck of this flask-like bulb is drawn out to a fine tip. When all the air is displaced from the bulb, and the substance is completely vaporized, the tip is sealed off in a flame. The temperature of the bath is recorded, also the barometric pressure. After cooling, the weight of the substance in the bulb and the capacity of the latter are accurately determined, and from these data the molecular weight can be calculated. This method, while simple in principle, is nevertheless tedious in practice.

A much more useful method for general purposes is that of *Victor Meyer*, in which the volume of a known weight of vapour is ascertained by finding how much air is displaced in a closed apparatus when the substance changes to a vapour.

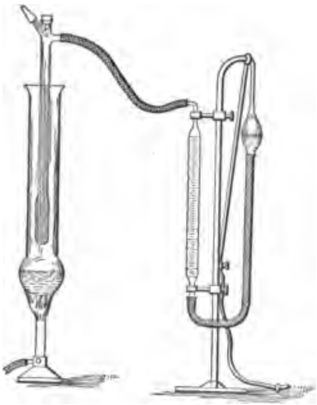

FIG. 15.

The apparatus,[1] as shown in the figure, consists of an elongated bulb continued above into a long neck closed at the top by a rubber stopper; from the neck passes a side tube which is connected by heavy rubber tubing with a gas burette. The bulb is suspended in a wide tube having a bulb-like expansion at its closed end (the upper two thirds of this tube should be wrapped with asbestos paper) and which contains some liquid with a boiling-point 40°–50° above the vaporization temperature of the substance.

EXPERIMENT. Fill the bulb of the outer tube two thirds full of distilled water; suspend the inner tube in it by means of a cork (this will have to be cut in two and then wired together again). By means of this cork also hang a thermometer in the steam-chamber and insert a bent glass tube as a steam-vent. Now boil the water (start the heating very gradually). When the thermometer registers a constant temperature, i.e., the boiling-point of the water,[1] connect the side tube with the gas burette and cork the inner tube tightly with a rubber stopper. Bring the water in the burette and in the reservoir to exactly the same level. If there is no variation from this level for 5–10 minutes the apparatus is ready for making an estimation. To do this remove the stopper of the inner tube and place in position (supported by the glass rod which fits the extra branch tube and extends into the neck of the main tube, see fig. 15) a little sealed glass bulb containing a known weight of pure chloroform (the bulb having been weighed before and after filling). Fit the stopper tightly, and wait a few minutes to determine whether the volume of the air in the apparatus remains constant (as indicated by the level of the liquid in the burette). When constant, fill the burette exactly to the cock by raising the reservoir after having brought the burette into communication with the outer air by means of a two-way cock (either the cock of the burette or one specially inserted in the rubber tubing connection). Then close the cock, so that the burette communicates only with the air of the system. Now drop the bulb to the bottom of the Victor Meyer tube by pulling the rod. Some glass wool has been put into the bottom of the tube to prevent injury. Vapour forms and air is pushed over into the burette. Level up the water in the burette with that in the reservoir. When the level remains absolutely constant for 10–15 minutes, close the cock of the burette. Measure the volume of the air displaced into the burette in exactly the same way as in nitrogen estimations (see p. 30), correcting for temperature, also for aqueous (see Appendix) and barometric pressure, and convert to the volume at 0° and 760 mm. (see p. 35). To make the calculation divide 22400 (22.4 L.) by the number of cubic centimetres of air displaced, and multiply this quotient by the weight of the chloroform vaporized; the product gives the weight of a gram-molecule of the substance, and the same figures express the molecular weight.

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[1] An excellent modification of this apparatus has been made by Bleier and Kohn, by which, instead of measuring air-displacement, the increase of pressure (the volume of gas in the apparatus being constant) due to the vaporization is measured by means of a mercury manometer. Before making an estimation the air-pressure in the apparatus is lowered by a suction-pump.

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[1] Boiling-point at 735 mm. barometric pressure is 99.1°, at 740 mm. 99.3°, at 745 mm. 99.4°, at 750 mm. 99.6°, at 755 mm. 99.8°, and at 760 mm. 100°.

THE NATURE OF SOLUTIONS. OSMOTIC PRESSURE.

In their physical properties solutions are very different from gases. In attempting to apply gas laws to substances in solution it is evident that other methods than those used in the case of gases must be adopted to measure the pressure of the dissolved substance. We measure the pressure of a gas by means of a manometer, but it is obviously impossible to measure the pressure of a dissolved substance by the same means, for the only pressure which the manometer can record is that of the solution against the walls of its container. In the case of a gas the molecules are suspended in a vacuum; in the case of a solution they are suspended in a solvent; the solvent of a solution is, therefore, analogous to the vacuum in which the gaseous molecules are suspended. For purposes of analogy is there any means by which the pressure of one gas suspended in another gas may be determined?

The metal palladium when heated to 200° allows hydrogen, but no other gas, to diffuse through it. If, therefore, a small vessel of heated palladium containing nitrogen be suspended in a confined atmosphere of hydrogen, hydrogen will diffuse into the vessel, but no nitrogen will diffuse out. In consequence of this the pressure inside the palladium vessel will become greater than that outside, and the difference between the two at the end of the experiment will represent the pressure of the nitrogen. The figure shows a piston working freely in the palladium box; hydrogen passing into the nitrogen chamber (indicated by arrows) increases the pressure on the under surface of the piston so that the latter moves upward.

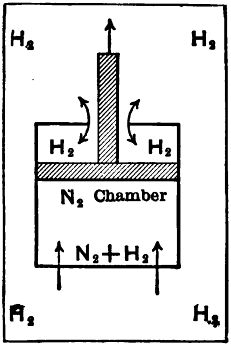

FIG. 16.

This gives us an indication of how it may be possible to measure the pressure of a dissolved substance, for in the above experiment we can conceive of the nitrogen as being in solution in hydrogen; indeed, to make the case still plainer, we can start the above experiment with a mixture of hydrogen and nitrogen inside the palladium vessel and measure increase of pressure.

This experiment shows us that if we could but obtain a membrane allowing only one of the constituents of a solution (i.e., the solvent) to pass through it, then we could measure the pressure which the other constituent (i.e., the solute) exercises. An example of such a membrane is a film of copper ferrocyanide. Since this film of copper ferrocyanide is too fragile to exist unsupported, it may be deposited in the pores of a porous cell (such as is used for electric batteries), and the following method may be used in preparing it.

A fine-grained porous cell, about four inches long and one inch inside diameter, is closed with a perforated rubber stopper, through which passes a glass tube connecting with a suction-pump. The cell is placed in water, and the water is sucked through the pores; then in acid, then in water again. By this means the pores of the cell are thoroughly cleaned. When clean, the cell is placed in a 15 per cent solution of potassium ferrocyanide, and suction is maintained until the pores are completely filled. The inside and the outside of the cell are then thoroughly washed with distilled water, after which it is immersed for several hours in a 25 per cent solution of copper sulphate. The copper sulphate reacts with the potassium ferrocyanide in the pores of the porous pot, so that a fine precipitate of copper ferrocyanide is deposited. After washing in water the cell is ready for use.

If a solution of cane sugar be placed inside such a cell and this be suspended in water, the latter will pass into the cell and cause the volume of fluid in this to increase, so that, if a vertical glass tube be connected with the cell, fluid will mount up in it to a very considerable height; or if we connect a pressure-gauge (manometer) with the cell, we shall be able to measure the pressure instead of the increase of volume. If a gram-molecular[1] solution of cane sugar be employed, the pressure in the cell as recorded by the mercury manometer comes to be equal to that of 22.4 atmospheres. This pressure, however, can seldom be attained, for it is too great for the fine film of copper ferrocyanide to withstand.[2] The film of copper ferrocyanide ruptures, and an escape of the fluid takes place. The pressure thus demonstrated is called *osmotic pressure,* and a membrane of the nature described is called a *semi-permeable membrane.*[3] It has been found that the osmotic pressure of all gram-molecular solutions corresponds to a pressure of 22.4 atmospheres, which, it will be remembered, is the pressure of a gram-molecule of gas compressed to the volume of a litre. Knowing this, we can calculate what the pressure of any dissolved substance in solution will be. Thus, the pressure x of a 1 per cent solution of cane sugar may be calculated from the proportion : Molecular solution : 22.4 atmospheres : : 1% solution : x. Solutions which obey the laws of osmotic pressure most accurately are those of the strength of decinormal solutions.

These facts show us that the osmotic pressure of a solution must be analogous to the pressure of a gas;

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[1] By gram-molecular solution is meant the molecular weight of a substance in grams dissolved in an amount of solvent sufficient to make 1 L. of solution (Arrhenius).

[2] An actual pressure equal to 22.4 atmospheres has recently been observed by Morse and Frazer by using a specially constructed apparatus.

[3] Solutions of salts and other substances which become dissociated in solution do not behave according to this law (see p. 51).

the volume in both cases being easily measured, we are therefore in a position to test the gas laws in solutions.

1. According to Gay-Lussac's law, the osmotic pressure should be proportional to the absolute temperature. That this is so is proved by the following observation. A 1 per cent solution of cane sugar at 14.2° has an osmotic pressure of 510 mm. Hg, and at 32° of 544 mm. Hg. According to calculation it should be 540.6 mm. Hg (practically agreeing with the finding), thus

$$510 \times \frac{273+32}{273+14.2} = 540.6.$$

2. According to Boyle's law, the osmotic pressure should be directly proportional to the concentration of the solution—or, in other words, inversely proportional to the volume of the solution. By comparing the osmotic pressures of cane sugar solutions of varying strengths (at the same temperature, 14°) the following values have been obtained:

Per Cent Strength of Solution.	Osmotic Pressure in Millimetres of Mercury.	Pressure + Concentration.
1.0	535	535
2.0	1016	508
4.0	2086	520
6.0	3075	512

It will be seen that the law applies.

3. According to Avogadro's hypothesis, all equimolecular solutions (i.e., solutions in which the weights of the solutes in a given quantity of solution bear the same ratio to one another as the molecular weights of

those substances) ought to have the same osmotic pressure. As already stated, this has been found to be the case.

Theoretically, the measurement of the osmotic pressure would be a simple enough way of determining the molecular weight, but, in practice, the method cannot be used, because, unless elaborate precautions be taken, any considerable pressure in the cell mechanically ruptures the membrane, and so allows the fluid to leak and the pressure to fall. The method is of interest mainly because it shows us the striking analogy between a gas and a solution. It shows us that the osmotic pressure is virtually the same as the gaseous pressure which any substance would exert were it present as a gas in the same volume as that occupied by the pure solvent: that if the solvent were suddenly removed the dissolved molecules might be considered as remaining suspended as a gas.

Biological Methods for Measuring Osmotic Pressure. If, in the above experiment with cane sugar solution, instead of placing the cell in water we had placed it in a solution of cane sugar weaker than that contained in the cell, then the osmotic pressure would not be so great as in the previous case, because water would pass into the cell only until the strength of the solution came to be the same as that outside it. This fact leads us to an important conclusion, viz.: that the relative strengths of two solutions can be ascertained by seeing whether osmosis occurs between them when they are separated from one another by a semi-permeable membrane.[1]

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[1] This is true only for solutions of diffusible substances in the same solvent (water).

In the case of the copper ferrocyanide cell, above described, we could determine this fact by measuring the pressure inside the cell. If, however, we employ a closed sac of some semi-permeable membrane filled with one of the fluids, then we could, by suspending this sac in some other fluid, tell if osmosis had occurred, by seeing whether the sac became distended or the reverse. In the case of the red blood-corpuscles we have a structure analogous to this. The envelope of the corpuscles acts like a semi-permeable membrane; it allows water to diffuse through it, but not salts.[1]

Now a corpuscle contains a solution of salts and hæmoglobin, and if it be placed in a fluid containing in solution the same number of molecules as is contained in the fluid inside the corpuscle, then no osmosis will occur in either direction and the corpuscle will remain unchanged in volume. Such a fluid is said to be *isotonic* with the fluid inside the corpuscle. If the corpuscle be placed in a solution which is weaker than that contained in the corpuscle, then water will diffuse in and the corpuscle will distend and may ultimately burst. Such a solution is said to be *hypoisotonic.* If the corpuscle be placed in a solution which is stronger than that of its fluid contents, then water will diffuse out of the corpuscle, so that the corpuscle will shrink. Such a solution is called *hyperisotonic.*

This change in the volume of the corpuscle may be observed under the microscope, and a quantitative expression also of the change in volume of the corpuscle may be obtained by using an instrument called a hæmatocrit. This consists of a graduated narrow capillary tube, about seven centimetres long. At one end the tube is widened so as to give space in which the fluids may be mixed. Blood is drawn into the capillary by means of a syringe and its volume accurately measured. The pipette is then closed at each end by small, accurately fitting, metal plates held in position by a spring.

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[1] The corpuscles are, however, permeable for alcohols, free acids, and alkalies, ammonium salts and urea.

The tube is then placed horizontally in a rapid centrifuge and rotated so that the corpuscles are thrown to the outer end. The graduation mark at which the column of corpuscles stands is then noted.

In another tube a drop of the same blood is mixed with an equal volume of the fluid whose molecular concentration it is desired to determine. The exact amount of blood and fluid taken is read off from the graduations of the tube. The two fluids are then sucked into the wide part of the tube and mixed by means of a fine platinum wire. The tube is then closed and centrifuged. If the corpuscles stand at the same level as for blood alone, then we know that the solution is isotonic with the blood-corpuscles, which means that they must also be isotonic with the plasma. If the column of corpuscles be longer, then we know that their volume must have been increased, and that the fluid under examination is hypoisotonic. If the column of corpuscles be shorter, the solution is hyperisotonic.

MOLECULAR WEIGHT OF SUBSTANCES IN SOLUTION.

Is there then no easily measurable physical property of solutions which depends on their molecular concentration, and which will, therefore, bear a relationship to the osmotic pressure? It has been found that the temperature at which a solvent freezes is lowered when a substance is dissolved in it, and that the amount of this lowering, or *depression of freezing-point,* is proportional, not, in general, to the chemical nature of the substance, but to the number of molecules of substance dissolved in a given volume. (The same holds true for the elevation of boiling-point, but this method will not be described here.) This being so, it follows that all gram-molecular solutions in the same solvent must lower the freezing-point to an equal extent. The depression of freezing-point produced by a gram-molecular quantity of a substance dissolved in 1000 gm. of the solvent varies for different solvents:

	Depression of freezing-point.
For water	1.85°
" benzol	5.00°
" phenol	7.20°
" acetic acid	3.90°

These figures represent the depression of freezing-point produced by a gram-molecular solution[1] in the different solvents and are called their constants or *C*. They correspond, therefore, to an osmotic pressure of 22.4 atmospheres.

The apparatus in which the freezing-point determinations are made is known as Beckmann's. This consists of a large test-tube, to contain the substance, suspended in a somewhat larger test-tube, so as to form an air-jacket between the two tubes. The outer test-tube is placed in a freezing-mixture of iced water and salt contained in an earthenware jar (which has been wrapped round with flannel to diminish the heat-conduction). The freezing-mixture is stirred with a loop of wire as represented in the diagram. In the inner test-tube is suspended the bulb of a Beckmann thermometer. This thermometer does not give absolute readings of temperature as does an ordinary thermometer. It is used only for demonstrating the difference in temperature at which two solutions freeze, or with certain modifications it may be used to tell the different temperatures at which two solutions boil. Before using the thermometer for freezing-point demonstrations the meniscus of the mercury column must be adjusted so that it stands within the scale (high up) at the temperature at which the solvent used freezes or crystallizes. To make this adjustment the bulb of the thermometer is placed in iced water, and if it be found that there is too much mercury to bring the meniscus within the scale, then the upper end of the thermometer is tapped with the fingers so as to cause the mercury at the top of the reservoir, which is connected with the uppĕr end

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[1] Attention must be called to the fact that such solutions (a gram-molecule dissolved in 1000 gm. of solvent) will vary somewhat from a true gram-molecular solution (see p. 41), firstly, because with solvents other than water 1000 gm. is either more or less than 1000 c.c., and, secondly, because many substances on going into solution cause increase (a few cause decrease) of volume, for example, 1 gm. of cane sugar dissolved in 100 gm. of water gives 100.6 c.c. of solution. In taking the weight of the solvent instead of the volume of the solution, Raoult's example has been followed by chemists.

An interesting explanation of the fact that *C* is quite different for different solvents is furnished in Raoult's extension of his law: if a gram-molecule of a compound be dissolved in 100 gram-molecules of solvent (except water), the freezing-point of the latter will be depressed by about 0.62°.

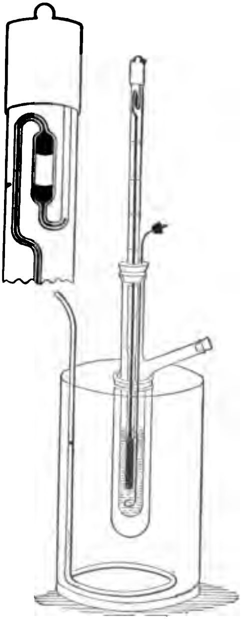

FIG. 17.

of the thermometer tube, to fall to the bottom and so to become disconnected from the mercury column in the thermometer tube. Should the meniscus of mercury stand below the scale at the freezing-point of water, or of the other solvent used, then the thermometer must be inverted, and, by tapping, more mercury can be added to that in the tube.

For making the actual freezing-point determination the inner tube of the apparatus is partly filled with the solution under examination so that the latter comes a little above the bulb of the thermometer (see fig. 17). The tube is then placed directly in the freezing-mixture until the mercury, having fallen to its lowest level, begins to rise again, after which the tube is removed from the freezing-mixture and placed in the larger test-tube, as before described. The cooling is then proceeded with until the meniscus of mercury stands at a constant level. During cooling, the fluid is kept constantly in motion by means of a platinum wire, bent into a loop as shown in the diagram. The reading is taken whenever constant and compared with the reading obtained when pure water (or whatever other solvent is used) is frozen. This difference is designated by Δ.[1]

Since this constancy of C, for any given solvent, is the point on which the method depends, the following experiment should be performed to demonstrate that for water C has the value given to it above.

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[1] Care should be taken that the supercooling is not excessive. If this be so, a correction is necessary. For aqueous solutions 1.25% of Δ is subtracted from the observed reading for each degree centigrade of supercooling.

Experiment. Weigh out a quantity of pure dry urea corresponding to one tenth its molecular weight in grams (i.e., 6 gm.); dissolve this in 100 c.c. of distilled water in the measuring flask at the temperature of 15°. Compare the freezing-point of this solution, corrected for supercooling, with that of pure water. It will be found to freeze almost exactly at 1.85° lower than that of water.

In determining the molecular weight of any substance we must first of all choose the most suitable solvent for it, and, in an accurately weighed quantity of this, dissolve an accurately weighed quantity of the substance under examination. Knowing what C for our solvent is,—in other words, through how many degrees centigrade the freezing-point of our solution would be lowered were a gram-molecular quantity per 1000 gm. of solvent taken,—if we find the freezing-point actually lowered to a less extent than this, we know that less than a gram-molecule must have been dissolved, the actual amount less than this being proportional to the difference from C recorded by the thermometer. In other words, the depression observed, represented by Δ, is to C as the strength of the solution used $\left(\frac{\text{weight of substance}}{\text{weight of solvent}}\right)$ is to that of a gram-molecular solution (or rather a solution containing a gram-molecule dissolved in 1000 gm. of solvent, see foot-note, p. 46).

$m=\frac{S}{L}\times\frac{C}{\Delta}$, where S equals the weight of substance used in grams; L, the weight of solvent in grams. $\frac{S}{L}$,

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when solved, gives a decimal fraction expressing what part of 1 gm. of the substance is dissolved in 1 gm. of solvent; therefore, to calculate the gram-molecule (the amount dissolved in 1000 gm. of solvent), m must be multiplied by 1000, and M equals the *molecular weight* in the equation $M = \frac{S}{L} \times \frac{C}{\Delta} \times 1000$. For example, let us take the determination in the following experiment.

Experiment. Make an accurate 1 per cent solution of pure cane sugar, estimate Δ; this will be found to be about 0.054°. The molecular weight of cane sugar is, therefore, $M = \frac{1}{100} \times \frac{1.85}{.054} \times 1000 = 342.5$. From its formula, $C_{12}H_{22}O_{11}$, it should be 342.

IONIZATION.

The method is not, however, applicable to all substances, even though they be readily soluble in the above-mentioned solvents. This is on account of the fact that in the case of those the extent to which a gram-molecular quantity per 1000 gm. of solvent lowers the freezing-point is greater than C. Practically all metallic salts and most acids and bases when in aqueous solution are included in this category. To demonstrate this let us determine the depression of freezing-point produced by a gram-molecular solution of sodium chloride.

Experiment. Weigh out one tenth the molecular weight of pure sodium chloride in grams and dissolve, as in the case of urea, in 100 c.c. of pure distilled water. Determine the depression of the freezing-point in Beckmann's apparatus. It will be found to be considerably greater than 1.85 (viz., about 3.35).

Knowing that 1.85 is Δ for a gram-molecular solution, it is easy to calculate how many gram-molecules per litre (X) a Δ of 3.35 will represent, thus:

$$1.85:1::3.35:X; \quad X=1.8.$$

To ascertain the actual osmotic pressure of the sodium chloride solution we must accordingly multiply 22.4 atmospheres by 1.8. This gives us about 40 atmospheres. This factor is known as the *isotonic coefficient* and is represented by the letter i.

What then is the cause of this deviation from the law? The answer to the question is furnished by comparing the *electrical conductivity* of the two classes of solutions. Solutions of those substances which obey the above law will be found to be bad conductors of electricity—*non-electrolytes,*—whereas solutions of those substances which do not obey it will be found to be good conductors—*electrolytes.* This discovery, viz., that solutions which conduct electricity appear, from the determination of Δ, to have a greater number of molecules than those which do not conduct, has led chemists to the conclusion that certain of the molecules in such solutions must split up into smaller molecules, called *ions*, and that it is only when this *dissociation* of molecules into ions takes place that it is possible for the solution to conduct electricity. In fact, our whole conception of the conduction of electricity in solutions is based on this hypothesis. It is supposed that every molecule of substance is charged with positive and negative electricity, which in the intact molecules so neutralize one another that we do not appreciate either. When these molecules are suspended in solution, however, they show a greater or less tendency to split up into ions, one set of which carries positive electricity and the other negative electricity. These ions wander about the solution much as if they were independent molecules.

When an electrical current is passed through a solution which has undergone dissociation into ions, the ions tend to collect at the two poles and yield up their electrical charges. Those which collect around the positive element or anode are called *anions*, and those collecting around the negative element or kathode are called *kations*. Anions are charged with negative electricity, and kations with positive electricity. Examples of anions are oxygen and the acid portion of salts, for example SO_4, Cl, etc.; the kations include hydrogen and metals.

When solutions of acids undergo ionization, the kation H is that which confers the acidic properties to the solution. An un-ionized acid does not act like an acid; for example, H_2SO_4 dissolved in toluene does not ionize and will not give off hydrogen in the presence of zinc. On the other hand, hydrogen itself, as the gas or in solution, shows no acid properties. We must assume, therefore, that the hydrogen ion is something different from the hydrogen atom. The same is true for other ions: they are not the same as the free elements or groups of elements; they are particles with opposite electrical charges which behave like molecules.

It is usual to designate the various ions by their symbols, affixed to which is the sign $^{\cdot}$ for kations (e.g., $H^{\cdot}$, $Na^{\cdot}$, etc.) and $'$ for anions (e.g., Cl', NO_3', etc.). Some ions must carry two or more units of electrical charge, however, for otherwise in the case of such a substance as H_2SO_4 there would be an excess of positive electricity in the molecule. The ion SO_4 must therefore carry two charges of negative electricity and be represented by the sign SO_4''. The valence of the ion usually agrees with the number of unit charges of electricity which it carries.

The isotonic coefficient therefore expresses the degree to which the molecules have become split up into ions. For molecules which can yield only two ions it cannot be greater than 2, but for those splitting into more than two ions it may exceed this number. In the concentration of a 1 per cent solution it is 1.82 for KCl, 1.67 for KNO_3, 2.11 for K_2SO_4, 2.18 for Na_2CO_3, and so on.

The amount of dissociation that a salt or acid undergoes in solution depends very largely upon the dilution: the greater the dilution, the greater the dissociation, and therefore the higher the isotonic coefficient.[1] For example, the isotonic coefficient of a 0.27 per cent solution of sodium chloride is 2, as against 1.9 for a 1 per cent solution.

Occasionally, when a substance is dissolved, instead of dissociation there occurs a fusion of several of the molecules. In such a case the freezing-point or boiling-point method would give too high a molecular weight. This tendency to form complex molecules most frequently manifests itself with organic substances containing hydroxyl or cyanogen groups, and when chloroform or benzol is the solvent.

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[1] For example, a solution of 0.03618 gm. HCl per litre $\left(\text{about } \frac{N}{1000}\right)$ is completely dissociated.

COLLOIDAL SOLUTIONS.

When solutions are dialysed (see p. 17) it is found that certain substances in solution diffuse through the parchment membrane into the water outside the dialyser, while others do not. The former are called *crystalloids*, and the latter *colloids*. Of these it is only the crystalloids that obey the laws above described. Colloidal solutions have practically no osmotic pressure. From a bio-chemical point of view, however, such solutions are of vast importance, since most of the tissue fluids contain colloids in solution. Colloidal solutions may exist in two forms, as liquids (called *hydrosols*) and as jellies (called *hydrogels*).[1] A hydrogel allows crystalloids to diffuse through it as readily as through water.

The essential feature of colloidal solutions is the large size of the molecules or aggregates of molecules. These are especially large in hydrogels, but they may be broken up into smaller aggregates by warming; hence a hydrogel becomes a hydrosol by the aid of heat. These molecules (or aggregates), it is claimed, can often be seen, or at least their presence can be revealed, by the use of the ultra apparatus. By means of this an intense beam of light is thrown through the solution, and examination is made with a very high-power microscope placed at right angles with the path of the light. The molecules so divert the light that some of its rays pass into the microscope. Many colloidal solutions, however, do not influence the beam of light, so that it is improbable that colloidal solutions are mere suspensions of the colloid in water, as some have supposed.

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[1] The terms hydrosol and hydrogel apply only to aqueous solutions. Colloidal solutions can be produced with other solvents than water.

The following are three of the most important properties of colloidal solutions:

1. Their absorptive power both for dissolved substances and for gases. Thus when a colloidal solution of ferric hydroxide is shaken with a solution of arsenious acid, the latter is taken up by the ferric hydroxide. On this account ferric hydroxide is the antidote to use in arsenical poisoning. The presence of colloids (proteid or dextrin) in beer greatly increases its power of taking up carbon dioxide gas.

2. When an electric current is passed through a mixed colloidal solution some colloids migrate to the anode, others to the kathode. All the molecules of a given colloid migrate to the same pole. They therefore behave like electrically charged particles, and this electricity being of the same sign, it causes the molecules in a colloidal solution to repel one another and therefore to keep apart.

3. When mixed with electrolytes or with other colloids they are readily precipitated. The precipitating power of the electrolyte seems to depend upon the electrical charge of its ions. This electricity neutralizes

that of some of the colloidal particles, so that they do not now repel one another, and in consequence they come together to form larger aggregates which are precipitated. This explains the precipitation of proteids by neutral salts, etc. When two different colloidal solutions are mixed together in proper proportion a precipitate forms, the precipitate consisting of both colloids. The process which ensues in this case is one of absorption of one set of particles by the other set.

MOLECULAR WEIGHT DETERMINATION BY ANALYSIS OF DERIVATIVES.

The molecular weight of a substance can also be deduced from a *quantitative analysis of its derivatives.* This method is most easily applied to acids and bases. Take, for example, a simple acid, such as acetic. By analysis, its formula might be $C_2H_4O_2$, or any multiple thereof. By forming its silver salt and estimating the amount of silver in it, this will be found to be 64.6%. Now, knowing that the atomic weight of silver is 107.9 and that it is monovalent, and having ascertained that only one silver acetate occurs (showing that the acid is monobasic), we can see what formula agrees with this proportion of silver in silver acetate. If we take $C_2H_3O_2Ag$ as the formula, the per cent of silver will be $\frac{107.9}{166.9}\times100=64.6\%$, whereas if $C_3H_5O_3Ag$ is the proper formula, there would be 54.8% of silver; therefore the first formula is correct. In the case of bases, their chlorplatinates have been found to be the most suitable compounds to form for this purpose.

CHAPTER V.

FORMULÆ, EMPIRICAL AND STRUCTURAL. ISOMERISM.

A KNOWLEDGE of the percentage composition and of the molecular weight of a substance, as we have seen, enables us to assign to it a formula indicating the number of atoms of each element present in the molecule. This is called the *empirical formula*. But it often happens that several organic substances with very different properties may have the same empirical formula. For example, there are no fewer than eighty-two compounds with the empirical formula $C_9H_{10}O_3$. Such bodies having the same empirical formula are called **isomers**, or, more particularly, *metamers* (same percentage composition and molecular weight), in contrast to *polymers*, which have the same percentage composition but different molecular weights. It is evident, therefore, that a more detailed formula is necessary—a formula, namely, in which the relations of the various atoms to one another (i.e., the grouping of the atoms) are indicated. Such a formula is called the *structural formula*. It is ascertained by acting on the substance with reagents which decompose it into simple bodies that can be identified; in other words, we must tear the molecule apart. After some knowledge has been gained as to what simpler groups of atoms the body is composed of, an attempt is made to build up the substance by causing the simpler groups to unite together, i.e., by synthesizing the substance. If the synthesis is successful, the structure of the molecule is proven.

We see then that the structural formula is not only a graphical expression of the actual number of the various atoms present in a molecule of the substance, but it is also an epitome of the more important reactions of the substance.

In the chapters which immediately follow this one, the methods by which the various facts indicating the structure of the molecule are discovered will be fully explained (see especially acetic acid, p. 116). When we come to study the more complex substances, we shall find that even the structural formula does not always suffice to differentiate the substance, since, indeed, there may be several bodies having the same structural formula. In such cases it is supposed that the cause of the difference lies in the order of arrangement of the atoms in space. This subject will be found described in connection with lactic and tartaric acids (pp. 167 and 174).

Before starting with a systematic study of the compounds of carbon the student should bear in mind the extreme importance of the structural formula; he should never allow one to pass him without thoroughly understanding why it is so written. If he conscientiously follows this advice, he will soon find that organic chemistry is by no means the uninteresting and disconnected subject so many students think it to be.

SYNOPSIS OF CHAPTERS I–V.

Determination of the Chemical Character of an Organic Compound.

1. PURIFICATION.
    - (*a*) Methods.
    - (*b*) Tests of purity.
2. IDENTIFICATION.
    - (*a*) Physical properties.
    - (*b*) Elementary analysis.
3. EMPIRICAL FORMULA.
    - (*a*) Elementary analysis.
    - (*b*) Molecular weight determination.
4. STRUCTURAL FORMULA.
    - (*a*) Reactions to detect presence and relative placing of atoms and groups of atoms in the molecule.
    - (*b*) Synthesis of the molecule.

CHAPTER VI.

PRELIMINARY SURVEY OF ORGANIC CHEMISTRY.

Before attempting to study the various organic substances individually, it is essential that we possess a general idea of their relationships to one another. Their number is so great that, did we attempt to remember the properties and reactions of each organic substance separately, we should utterly fail, and should, moreover, probably overlook one of their most important characteristics in contrast with inorganic substances, viz., their transmutability into other organic compounds. In inorganic chemistry it is impossible to convert the compounds of one element into those of another element, except by substituting the elements. Each element has its own fixed chemical properties and compounds. In organic chemistry, on the other hand, as remarked above, we may consider all our substances as compounds of the element carbon and as being, therefore, convertible into one another.

As is natural, we select as our basis of classification the very simplest organic substances, namely, those which contain carbon along with one other element. From our studies in inorganic chemistry we know that there are several elements with which carbon may be thus combined, e.g., with oxygen in CO_2, with sulphur in CS_2, etc. We do not, however, consider these as organic compounds, the simplest organic compounds being those in which carbon is combined with hydrogen or with nitrogen.

In union with nitrogen, carbon forms *cyanogen* (CN (in the free state C_2N_2), which is the lowest member of a group of compounds including hydrocyanic acid, HCN, cyanic acid, HCNO, sulphocyanic acid, HCNS) and the substituted ammonias.

In union with hydrogen, carbon forms the so-called *hydrocarbons* (i.e., hydro(gen) carbons). Practically all the remaining carbon compounds may be considered as derived from these.

The quantitative relationship between C and H in hydrocarbons is variable, so that we are enabled to subdivide hydrocarbons into several groups. If we express the hydrogen in terms of its proportion to carbon, we shall find that all the hydrocarbons group themselves into several series, four of which are of importance. The general formulæ for the four series or groups are as follows:

$$(1)\ C_nH_{2n+2} \qquad (3)\ C_nH_{2n-2}$$
$$(2)\ C_nH_{2n} \qquad (4)\ C_nH_{2n-6}$$

(n designating the number of C atoms).

It will, moreover, be found that it is to the first and fourth of these groups that the great majority of hydrocarbons belong.

If, now, we investigate the behaviour of the members of these four groups towards hydrobromic acid, we shall find that members of the first and fourth groups do not readily react, whereas those of the second and third do;

indeed, that these directly combine with the reagent by addition, i.e., without chemical substitution. We may, therefore, further subdivide our four groups into two, viz., *saturated* (1st and 4th) and *unsaturated*[1] (2d and 3d).

Of the two *saturated* groups it will be found that the members of the 4th group have an aromatic odour, whereas those of the 1st do not. The members of the 4th group are hence often styled *aromatic compounds*, and on account of the fact that the members of the 1st group are very resistant towards chemical reagents they are called *paraffins* (*parum affinis*).

On account of their properties, then, we may amplify our classification into paraffins (1st group), unsaturated compounds (2d and 3d), and aromatic bodies (4th).[2] Compounds of the first three groups make up the ALIPHATIC OR FATTY DIVISION of organic chemistry.

The compounds and derivatives formed by the various hydrocarbons of each of these groups are, in general, analogous, although the reactions by which they are produced may differ somewhat. If we understand the chemistry of the most important derivatives of one hydrocarbon in each group we shall be able to infer approximately what the derivatives and reactions of all the other members of the group will be; and further, when we come to study the hydrocarbons of the other groups we shall find many of their compounds quite similar to those already met with.

From these preliminary remarks it will be evident that we must first of all take one group, and, having shown the relationship of its various members to one another, then study carefully the derivatives of some one or two of these members.

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[1] Only unsaturated compounds can form addition products.

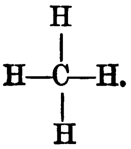
[2] The groups are also sometimes named from the lowest member of each, e.g., methane group, benzene group, etc.

Let us take the **paraffins**. They have the general formula C_nH_{2n+2}. The following is a list of the most important members:

Methane,	CH_4	Butane,	C_4H_{10}
Ethane,	C_2H_6	Pentane	C_5H_{12}
Propane,	C_3H_8	Hexane,	C_6H_{14}

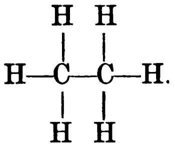
It will be noticed that each differs from the one preceding it by CH_2. They all form the same kind of derivatives, differing from one another again by CH_2· thus the hydroxide or alcohol of methane has the formula CH_3OH, and of ethane C_2H_5OH. Such a series is called an *homologous series* (*cf.* nitrogen oxides series).

Let us consider why it should be that the increase of complexity is by CH_2. To understand this we must remember that C is considered to have a valence of four; that, in other words, an atom of it can combine with four atoms of a monovalent element such as H, and that each of these valence bonds has exactly the same combining value. We may therefore write the structural formula for methane as



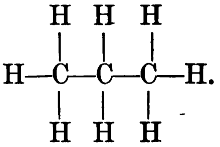
$$\begin{array}{c} H \\ | \\ H{-}C{-}H. \\ | \\ H \end{array}$$

When two methane molecules fuse together a hydrogen atom of each disappears and the liberated valence bonds unite as represented in the formula



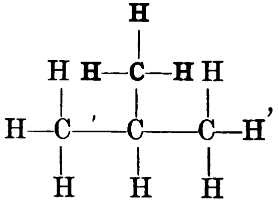
$$\begin{array}{ccccccc} & & H & & H & & \\ & & | & & | & & \\ H & — & C & — & C & — & H. \\ & & | & & | & & \\ & & H & & H & & \end{array}$$

Since each of the four valence bonds of C has the same value it will be obvious that only one propane can exist: that we can write only one structural formula for it, viz.,

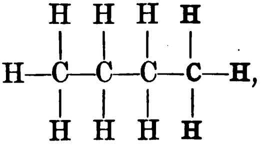


$$\begin{array}{ccccccccc} & & H & & H & & H & & \\ & & | & & | & & | & & \\ H & — & C & — & C & — & C & — & H. \\ & & | & & | & & | & & \\ & & H & & H & & H & & \end{array}$$

But we may have two varieties of the next member of the series, viz., butane, for, in adding an extra CH_3 group to propane, we may add it either to the central C atom of the chain or to one of the end ones,



$$\begin{array}{ccccccccc} & & & & H & & & & \\ & & & & | & & & & \\ & & H & & H—C—H & & H & & \\ & & | & & | & & | & & \\ H & — & C & — & C & — & C & — & H, \\ & & | & & | & & | & & \\ & & H & & H & & H & & \end{array}$$

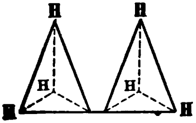


$$\begin{array}{ccccccccccc} & & H & & H & & H & & H & & \\ & & | & & | & & | & & | & & \\ H & — & C & — & C & — & C & — & C & — & H, \\ & & | & & | & & | & & | & & \\ & & H & & H & & H & & H & & \end{array}$$

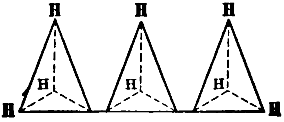
and the properties of the corresponding body will vary accordingly; in other words, it makes a difference when the extra CH_3 group is tacked on to a C atom in union with two H atoms (as is the case with the central atom), and when on to one with three H atoms (as in the case of an end atom).

When the substitution occurs in the centre of the chain the resulting body is called an *iso*-compound; when at the end it is *normal.* Such an *iso*-compound therefore contains a branched chain. Now, this *isomerism* applies not only to the methyl derivatives of propane—for butane may be considered as such—but also to all its derivatives, e.g., chlorides, hydroxides, etc.

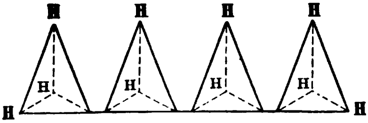
By using models instead of formulæ these points can be still more clearly demonstrated: thus we may consider C as occupying the core of a tetrahedron (made



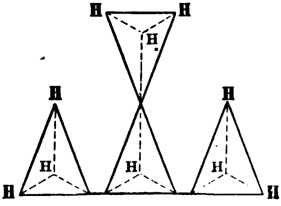
Ethane



Propane



Normal butane



Isobutane

of wood), the four solid angles of which represent monovalent combining affinities, these angles being covered in the model by pyramidal tin caps representing H atoms (see fig. 22, p. 174). By removing an H cap from two models of methane and joining the two tetrahedra together by the bared angles we obtain the model of ethane. And if by removing another H cap from ethane we unite three such tetrahedra we obtain the model of propane. It does not matter which of the H caps we remove in these manipulations; the resulting ethane or propane models are always the same. When we proceed to add another tetrahedron to propane, however, it will be evident that this can be done in either of two ways, by attaching it either to one of the end tetrahedra or to the central one; in the former case the model will represent normal butane, and in the latter isobutane; and so with the other homologues.

We may also describe this progression from one hydrocarbon to the next higher as being due to the replacement of the H atoms of the former by the group CH_3, called *methyl.*

Now we may proceed with the **derivatives of the paraffins**. These are produced by the replacement of one or more of the H atoms of the simple hydrocarbons by various elements or groups of elements. Since, as explained, these derivatives are, in general, the same for each member of a series, we may choose any one of these and confine our attention for the present to its derivatives, remembering always that the corresponding derivative of any other member of the series will differ from it by just as many CH_2 groups as did the original hydrocarbons differ from one another.

In inorganic chemistry the halogen compounds, the oxides, and the hydroxides are among the most important compounds of an element, and the same applies to the hydrocarbons: each has halogen derivatives, oxides (ethers), and hydroxides (alcohols). Beyond these, however, the analogy breaks down, for whereas an inorganic hydroxide is an ultimate product and cannot be further oxidized, an organic hydroxide (or alcohol) can be oxidized so as to yield various substances according to the extent of the oxidation and the nature of the alcohol started with. We may, therefore, classify our derivatives thus:

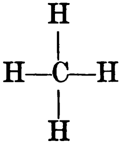
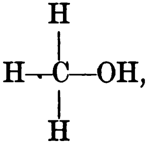
Halides.
Oxides or ethers.
Hydroxides or alcohols.
Oxidation products of alcohols.

Halides. When the paraffins are brought into contact with chlorine, substitution of one or more of the H atoms occurs. Thus, taking methane, we may have monochlormethane, dichlormethane, trichlormethane (chloroform), and tetrachlormethane. In connection with the monohalogen substitution products it should be pointed out that they may be considered as derived from a halogen acid, the H of the acid having been replaced by a hydrocarbon minus one of its H atoms. The general term for all such groups is *alkyl*, and the specific names for the alkyls are methyl (CH_3-), ethyl (C_2H_5-), propyl (C_3H_7-), and so on. An alkyl is, therefore, analogous with a monovalent element or with NH_4-.

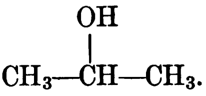
Halogen atoms may likewise displace one or more of the H atoms of the alkyl radicle when this latter is already in combination with some other substituting group. Thus, chloral is trichloraldehyde, CCl_3CHO, aldehyde being CH_3CHO.

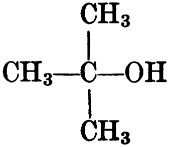
Oxides (or ethers). Since oxygen combines with two atoms of a monovalent element, as in sodium oxide, Na_2O, the lowest alkyl oxide will have the formula

$\begin{matrix}CH_3\\CH_3\end{matrix}\!>\!O$. To this group belong the ethers, common ether being $\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\!>\!O$.

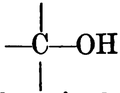
Hydroxides (or alcohols). When one of the H atoms of methane is replaced by hydroxyl, OH, methyl alcohol is formed. Thus  $\begin{matrix}&H&\\&|&\\H-&C&-H\\&|&\\&H&\end{matrix}$ becomes  $\begin{matrix}&H&\\&|&\\H-&C&-OH\\&|&\\&H&\end{matrix}$, and it does not matter which of the H atoms is thus replaced, the resulting compound being always the same.

The same is true for ethane and its alcohol, ethyl alcohol, CH_3-CH_2OH.

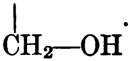
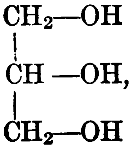
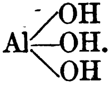
When we come to form the alcohol from propane, however, we encounter conditions analogous with those which exist when butane is formed from propane (see p. 65); we may add the OH group to a C atom of propane which is in combination with three hydrogen atoms or to one in union with two such, and the resulting product, as we have seen, will exhibit different properties. Consequently we have two forms of propyl alcohol. Of these the OH group in the one is attached at the end of the chain, $CH_3-CH_2-CH_2OH$; in the other it is attached in the middle of the chain,  $\begin{matrix}&OH&\\&|&\\CH_3-&CH&-CH_3\end{matrix}$. The former is called a *primary alcohol*, the latter a *secondary alcohol.*

In the case of butane, we may have the hydroxyl radicle at the end of the chain, $CH_3-CH_2-CH_2-CH_2OH$ (primary butyl alcohol); or attached to a C atom in the centre of the chain with one other H atom attached to it, $CH_3-CH_2-CH{<}\begin{matrix}OH\\CH_3\end{matrix}$ (secondary butyl alcohol); or —a third possibility—the hydroxyl radicle may be attached to a C atom which is not directly combined with any other H atom, thus  $CH_3-\underset{CH_3}{\overset{CH_3}{C}}-OH$ (tertiary butyl alcohol).

There are, therefore, three varieties of these alcohols:

1. Primary, containing the group $-CH_2OH$
2. Secondary, " " " $-CHOH-$
3. Tertiary, " " "  $-\underset{|}{\overset{|}{C}}-OH$

The essential chemical difference between these is that when oxidized they yield different products. These we shall consider immediately.

In all these alcohols only one hydroxyl radicle is present: they are analogous with hydroxides of monovalent elements such as sodium (thus NaOH is analogous with CH_3OH). Just as in inorganic chemistry, however, we may have hydroxides with two hydroxyls, e.g., $Ca{<}\begin{matrix}OH\\OH\end{matrix}$, so may we have alcohols with two hydroxyls, e.g.,  $\begin{matrix}CH_2-OH\\|\\CH_2-OH\end{matrix}$. Similarly, there are alcohols containing three hydroxyl groups, e.g.,  $\begin{matrix}CH_2-OH\\|\\CH\ -OH\\|\\CH_2-OH\end{matrix}$, which are analogous with  $Al{<}\begin{matrix}OH\\OH\\OH\end{matrix}$.

Alcohols, like hydroxides in general, have the power of neutralizing acids to form salts. Thus, sodium hydroxide reacts with HCl in accordance with the equation $NaOH + HCl = NaCl + H_2O$: and taking an alkyl hydroxide (alcohol) instead of an alkaline hydroxide, we have $ROH + HCl = RCl + H_2O$ (R = alkyl).[1] They can react in this way with organic acids, the resulting body being known as an ethereal salt (see p. 125).

An alcohol with only one hydroxyl group is called *monacid*,[2] because it can react with only one molecule of a monobasic acid; those with two such groups are called *diacid;* those with three are called *triacid.* The monacid alcohols are by far the most numerous; there is only one diacid alcohol (glycol) of importance and one triacid alcohol (glycerol).

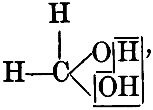
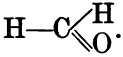
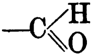
Oxidation Products of Alcohols. As has been mentioned (p. 69), the division into primary, secondary, and tertiary alcohols is warranted by the difference of their behaviour on oxidation.

Primary alcohols yield on oxidation aldehydes and acids.

Secondary alcohols yield ketones.

Tertiary alcohols, when oxidized, break up into lower compounds.

The oxidation products that we must consider are, therefore, aldehydes, acids, and ketones.

A. **Aldehydes.** When methyl alcohol, CH_3OH, is oxidized, one of the H atoms of the methyl radicle becomes replaced by hydroxyl, so that a body having the formula $CH_2(OH)_2$ would tend to be formed. But such a body having two hydroxyls directly attached to a C atom cannot exist, and it immediately breaks up, giving off water, thus:  $\mathrm{H{-}\overset{H}{\overset{|}{C}}}\genfrac{}{}{0pt}{}{\mathrm{O\boxed{H}}}{\mathrm{\boxed{OH}}}$, leaving a body having the formula  $\mathrm{H{-}C}\genfrac{}{}{0pt}{}{\mathrm{H}}{\mathrm{O}}$. This is an aldehyde, and the group  $\mathrm{{-}C}\genfrac{}{}{0pt}{}{\mathrm{H}}{\mathrm{O}}$ is known as the *aldehyde group.* The CO portion of this group is called *carbonyl.* Each hydrocarbon has a corresponding aldehyde.

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[1] Alcohols, however, are not really basic in the same sense as are metallic hydroxides.

[2] The terms mon*atomic* and mono*hydric* are also used.

B. **Acids.** When an aldehyde is further oxidized it absorbs oxygen and forms a body having the group COOH, which is called the *carboxyl group* (from carb[onyl hydr]oxyl) and is the characteristic acid group of organic compounds:

$$\underset{\text{(Formic aldehyde)}}{\mathrm{H{\cdot}CHO}}+\mathrm{O}=\underset{\text{(Formic acid)}}{\mathrm{H{\cdot}COOH}}.$$

The H atom of this carboxyl group can be replaced by an atom of a monovalent metal to form a salt, thus: $\mathrm{H{\cdot}COONa}$, sodium formate. Instead of a metal, an alcohol may replace this H atom, the resulting compound being called an ethereal salt, thus: $\mathrm{H{\cdot}COOC_2H_5}$, ethyl formate. Such an acid can form only one salt; it is *monobasic.*

If two carboxyl groups be present the resulting acid is *dibasic.* The lowest dibasic acid corresponding to the simplest diacid alcohol is oxalic, having the formula $\begin{array}{l}\mathrm{COOH}\\ |\\ \mathrm{COOH}\end{array}$. Like dibasic acids in general, these acids can form two series of salts, in one of which only one carboxyl group reacts, $\begin{array}{c}COOK\\ |\\ COOH\end{array}$ (acid potassium oxalate), and in the other, both, $\begin{array}{c}COOK\\ |\\ COOK\end{array}$ (neutral potassium oxalate). *Tribasic* organic acids also exist, but are unimportant.

C. **Ketones.** When a secondary alcohol is oxidized it forms a body having the group —CO—, which is called a ketone:

$$\underset{\text{(Secondary propyl alcohol)}}{CH_3—CHOH—CH_3} + O = \underset{\text{(Acetone)}}{CH_3—CO—CH_3} + H_2O.$$

THE NITROGEN DERIVATIVES are divided into three classes—cyanogen, ammonia, and nitro-compounds.

As we have inorganic cyanides, as KCN, so we have **organic cyanides,** as $CH_3 \cdot CN$, methyl cyanide.

There are several kinds of **ammonia derivatives.** One hydrogen atom of NH_3 may be replaced by an organic radicle, leaving the group NH_2, which is called the *amido- or amino-group.* Two hydrogen atoms may be displaced, leaving NH, called the *imido-group.* All three hydrogen atoms may be displaced, leaving only N; such compounds are called *tertiary bases.* Or we may have the hydrogens of ammonium (NH_4) in NH_4OH displaced, as in the *quaternary bases.*

The **nitro-compounds** have the group NO_2.

SULPHUR DERIVATIVES may take the place of oxygen in an alcohol or ether, giving **sulphur alcohols** (mercaptans), as CH_3SH, and **sulphur ethers,** as $CH_3—S—CH_3$.

Sulphonic acids contain the group SO_3H instead of carboxyl.

As MIXED COMPOUNDS we class (1) hydroxy-acids, (2) amino-acids, acid amides, and certain complex amido- and imido-compounds, and (3) carbohydrates. **The hydroxy-acids** contain one or more hydroxyls besides that in carboxyl.

The amino-acids contain both the NH_2 and COOH groups. **Acid amides** have the OH of carboxyl substituted by an NH_2 group.

The carbohydrates contain alcohol groups and one or more aldehyde or ketone groups.

Finally, UNSATURATED HYDROCARBONS, having the linkings $C{=}C$ and $C{\equiv}C$, and their derivatives, will conclude the chemistry of fatty compounds.

The last great division of organic chemistry, that of the AROMATIC OR BENZENE COMPOUNDS, can be considered but briefly in this book.

SYNOPSIS.

I. Fatty or Aliphatic Compounds.

A. SATURATED HYDROCARBONS.
Paraffins, C_nH_{2n+2}.
Paraffin derivatives.
1. *Halogen substitution products.*
2. *Oxides or ethers.*
3. *Hydroxides or alcohols.*
a. Monacid alcohols.
(1) Primary alcohols, group $—CH_2OH$.
Oxidation products $\begin{cases}\text{Aldehydes, —CHO.}\\ \text{Acids, —COOH.}\end{cases}$
(2) Secondary alcohols, —CHOH.
Oxidation product $\Big\{$ Ketones, —CO—.

        - (3) Tertiary alcohols, —COH.
    - *b.* Diacid alcohols.
        - Oxidation products $\left\{\begin{array}{l}\text{Aldehydes.}\\\text{Acids.}\end{array}\right.$
    - *c.* Triacid to hexacid alcohols.
        - Oxidation products $\left\{\begin{array}{l}\text{Aldehydes.}\\\text{Acids.}\end{array}\right.$
- 4. *Nitrogen derivatives.*
    - *a.* Cyanogen combinations.
    - *b.* Ammonia combinations (amido-group, NH_2; imido-group, NH, etc.).
    - *c.* Nitro-compounds.
- 5. *Sulphur derivatives.*
- 6. *Mixed compounds.*
    - *a.* Hydroxy-acids.
    - *b.* Amino-acids, acid amides, and other similar compounds.
    - *c.* Carbohydrates.

B. UNSATURATED HYDROCARBONS.
- 1. *Ethylenes,* C_nH_{2n} ($—C{=}C—$).
- 2. *Acetylenes,* C_nH_{2n-2} ($—C{\equiv}C—$).

C.[1]

II. Aromatic Compounds.

A. BENZENE HYDROCARBONS, C_nH_{2n-6}.

Benzene derivatives (see synopsis, p. 326).

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[1] As will be explained later, the group of cyclic hydrocarbons and the terpenes (see p. 235) is really an intermediate class of compounds between the fatty and the aromatic, and it would naturally be inserted in the synopsis after C. To avoid confusion we say nothing about these compounds in this chapter.

CHAPTER VII.

SATURATED HYDROCARBONS. THE METHANE SERIES.

Methane (CH_4) can be synthesized from the elements in several ways:

(1) A small quantity of CH_4 can be produced directly from the elements by passing a stream of hydrogen between the glowing carbon tips of an electric arc-light (see acetylene, p. 233).

(2) By producing carbon disulphide (CS_2) and hydrogen sulphide (H_2S), and allowing a mixture of them to act on heated copper:

$$CS_2 + 2H_2S + 8Cu = CH_4 + 4Cu_2S.$$

(3) By the action of water on aluminium carbide:

$$Al_4C_3 + 12HOH = 3CH_4 + 4Al(OH)_3.$$

THE PARAFFINS OR MARSH-GAS SERIES, C_nH_{2n+2}.

Having obtained methane, the other members of the series may be built up from it by first of all producing its halogen substitution products and then reacting on these with metals, thus:

$$\underset{\text{(Methyl iodide)}}{CH_3\boxed{I + Na}} + \boxed{Na + I}CH_3 = \underset{\text{(Ethane)}}{CH_3 \cdot CH_3} + 2NaI,$$

$$\underset{\text{(Methyl iodide)}}{CH_3\boxed{I+Na}} + \underset{\text{(Ethyl iodide)}}{\boxed{Na+I}C_2H_5} = \underset{\text{(Propane)}}{CH_3\cdot CH_2\cdot CH_3}\text{[1]} + 2NaI;$$

also with zinc methyl, thus:

$$2CH_3\boxed{I+Zn}\underset{\text{(Zinc methyl)}}{(CH_3)_2} = 2CH_3\cdot CH_3 + ZnI_2,$$

$$2C_2H_5\boxed{I+Zn}(CH_3)_2 = 2CH_3\cdot CH_2\cdot CH_3 + ZnI_2.$$

The paraffins may be prepared for general purposes (1) by decomposing the proper substitution product with nascent hydrogen, or (2) by heating an acid derivative with an excess of soda-lime:

$$\underset{\text{(Methyl iodide)}}{CH_3I} + 2H\text{[2]} = CH_4 + HI,$$

$$\underset{\text{(Sodium acetate)}}{CH_3\cdot COONa} + NaOH = CH_4 + Na_2CO_3.$$

Methane (marsh-gas), CH_4, occurs in nature as a gas arising from stagnant water where decomposition of vegetable matter is going on, as fire-damp in coal-mines, and as one of the constituents of natural gas. Its production by decomposition of vegetable matter can be brought about in the laboratory by inoculating water containing small suspended pieces of filter-paper (cellulose) with the microörganisms contained in sewerage. It forms an explosive mixture with air, hence the danger of having bare flames in coal-mines and the necessity for using the Davy safety-lamp. Fortunately the kindling temperature (i.e., the temperature at which it explodes) of this gas is high.

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[1] C_2H_6 and C_4H_{10} are also formed.

[2] The nascent hydrogen for such reactions as this may be obtained from a copper-zinc couple (made by heating together one part of powdered copper with three parts of powdered zinc and then cooling in a closed vessel). In the presence of a trace of acid (H_2SO_4) the couple readily yields nascent hydrogen. In the above reaction a mixture of the methyl iodide with alcohol and a drop of H_2SO_4 is brought into contact with the couple, drop by drop.

Natural gas is about ninety-five per cent methane; it also contains a little nitrogen and ethane. There are two hypotheses as to the production of natural gas, one that it is the result of decomposition of vegetable or animal matter, and the other that it is due to the action of water on metallic carbides (*cf.* aluminium carbide reaction). *Coal-gas* contains about forty per cent of methane.

Methane is a colourless, odourless, stable gas. When mixed with chlorine and exposed to direct sunlight it explodes:

$$CH_4 + 4Cl_2 = \underset{\text{(Carbon tetrachloride)}}{CCl_4} + 4HCl,$$

or when exposed to diffused sunlight it forms a mixture of monochlor- (CH_3Cl), dichlor- (CH_2Cl_2), trichlor- ($CHCl_3$), and tetrachlor-methane (CCl_4). The last is also called carbon tetrachloride.

Experiment. Dehydrate some sodium acetate by heating it in an evaporating dish with a small flame. Cool, mix 10 gm. with 40 gm. of soda-lime, and heat in a retort on a sand bath. By means of a delivery tube fitted to the retort, collect the evolved methane over water in the usual manner. Test its inflammability.

Ethane (C_2H_6), **propane** (C_3H_8), and **butane** (C_4H_{10}) are also gases at ordinary temperatures. The other paraffins are liquids or solids. Above butane the name indicates the number of carbon atoms in the formula. There is a regular gradation of physical properties from the lowest to the highest members of the paraffin series: the boiling-point, the specific gravity, and, with the higher paraffins, the melting-point increase as we ascend the series.

	Boiling-point.	Specific gravity.	Melting-point.
Methane, CH_4	−164°	0.415 (at −164°)	−184°
Ethane, C_2H_6	− 84.1°	0.446 (at 0°)	−172.1°
Propane, C_3H_8	− 44.5°	0.535 (at 0°)	− 45°
Butane, C_4H_{10}	+ 1°	0.600 (at 0°)	
Pentane, C_5H_{12}	36.3°	0.627 (at 14°)	
Hexane, C_6H_{14}	69°	0.6603 (at 20°)	
Tetradecane, $C_{14}H_{30}$	252°	0.775 (at 4°)	4°
Hexadecane, $C_{16}H_{34}$	287°	0.7758 (at 18°)	18°
Octodecane, $C_{18}H_{38}$	317°	0.777 (at 28°)	28°

The members of the series after methane are met with mainly in petroleum. American petroleum also contains a few sulphur derivatives. California petroleum contains some benzene hydrocarbons. To render petroleum suitable for commercial purposes, it is subjected to crude fractional distillation. The oils thus obtained are purified by successive treatment with sulphuric acid, caustic soda solution, and water. The lower fractions are distilled with steam; the distillate between 40° and 150° is *gasoline* (or naphtha), and that between 150° and 300° is *kerosene*. Gasoline and its products are mostly mixtures of C_6H_{14}, C_7H_{16}, and C_8H_{18}. From low-boiling gasoline can be obtained, by careful fractional distillation, cymogene, rhigolene, ligroin, and *petroleum ether*. High-boiling gasoline, called also benzine,[1] is used as a solvent in many industrial processes. Kerosene contains the paraffins from C_9H_{20} to $C_{16}H_{34}$. It should contain no gasoline, as the vapour of the lower hydrocarbons in a lamp would form an explosive mixture with air. Its flashing-point, tested in a manner similar to that described in the experiment below, tells us whether it contains any gasoline. The minimum flashing-point is regulated by law, varying from about 38° to 49°. The higher-boiling oils from petroleum are used as lubricants. *Vaseline* is a yellowish semi-solid product, while the commercial substance called *paraffin* is a white solid. Pennsylvania petroleum gives 8–10% naphtha, 70–80% refined oils, and 5–9% of solid products.

EXPERIMENT. Place the flashing-point apparatus (see fig. 18) containing 20 c.c. of kerosene in a large beaker two thirds full of water. Suspend a thermometer so that the bulb is in the kerosene. Heat the beaker slowly. Bubble air through the oil at frequent intervals, and test the vapour with a lighted match. Note the temperature when the *vapour* takes fire (the burning temperature of the oil is 40°–50° above the flashing-point).

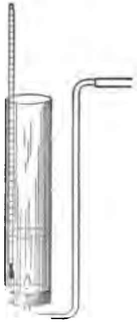

FIG. 18.

There are many isomers of the paraffins (see p. 65).

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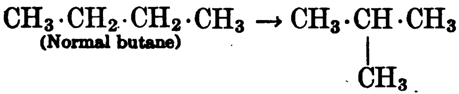
[1] Carefully distinguish from *benzene* (p. 242).

These *iso-compounds* are represented in their formulæ as having branched chains of carbon atoms instead of straight chains as in the normal compounds, and they possess properties quite different from those of the normal paraffins.

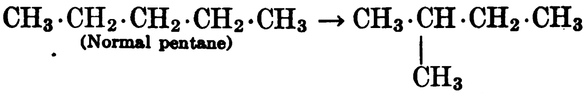
Isobutane is the iso-compound having the fewest carbon atoms (see p. 65):



$$CH_3\cdot CH_2\cdot CH_2\cdot CH_3 \rightarrow CH_3\cdot \underset{\underset{CH_3}{|}}{CH}\cdot CH_3$$

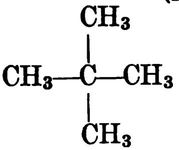
(Normal butane) **(Isobutane)**

Isopentanes. There are several pentanes:



$$CH_3\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_3 \rightarrow CH_3\cdot \underset{\underset{CH_3}{|}}{CH}\cdot CH_2\cdot CH_3$$

(Normal pentane) **(Isopentane)**



$$\begin{array}{c} CH_3 \\ | \\ CH_3—C—CH_3 \\ | \\ CH_3 \end{array}$$

(Neopentane)

The newer nomenclature designates these isomers as derivatives of methane; thus, isopentane is dimethyl-ethyl-methane, and neopentane is tetramethyl-methane.

CHAPTER VIII.

HALOGEN SUBSTITUTION PRODUCTS OF THE PARAFFINS.

IF only one hydrogen atom of the hydrocarbon is replaced by a halogen atom the compound is called an alkyl halide, because it consists of a halogen atom linked to an alkyl radicle, e.g., $CH_3{-}Cl$ (see p. 67).

The **alkyl halides** derived from methane are methyl chloride or monochlormethane, CH_3Cl; methyl bromide or monobrommethane, CH_3Br; methyl iodide or monoiodomethane, CH_3I.

General Methods of Preparation. (1) The chloride and bromide can be produced from methane by mixing chlorine or bromine with it and exposing the mixture to diffused sunlight

(2) All may be secured by acting on methyl alcohol with the proper halogen acid, in accordance with the following equations:

$$CH_3\boxed{OH+H}Cl = CH_3Cl + H_2O,$$

$$CH_3\boxed{OH+H}Br = CH_3Br + H_2O,$$

$$CH_3\boxed{OH+H}I = CH_3I + H_2O.$$

(3) Another method of obtaining them is by the action on methyl alcohol of PCl_3, PBr_3, and PI_3:

$$3CH_3OH + PCl_3 = 3CH_3Cl + P(OH)_3,$$
$$3CH_3OH + PBr_3 = 3CH_3Br + P(OH)_3,$$
$$3CH_3OH + PI_3 = 3CH_3I + P(OH)_3.$$

In a manner exactly similar to the last two methods, the ethyl halides can be derived from ethyl alcohol.

Some of the More Important Alkyl Halides.

Methyl chloride (monochlormethane), CH_3Cl, is a gas under ordinary conditions. It is readily liquefied, the liquid boiling at $-23.7°$. It has been used as a local anæsthetic by spraying the liquid on to the skin from a strong glass container. The rapid evaporation causes the abstraction of enough heat from the skin to result in freezing the latter.

Ethyl chloride (monochlorethane), C_2H_5Cl, is a liquid boiling at 12.2°. It is put up in glass or metal tubes, and is used for local anæsthesia in the same way as methyl chloride. It is beginning to be used also as a general anæsthetic,[1] being administered as a vapour by inhalation.

Ethyl bromide (monobromethane), C_2H_5Br, is a liquid resembling chloroform in odour, density, and physiological effect. It boils at 38.37° (at 37.1°–37.4° under 737 mm. pressure), and its specific gravity is 1.450 at 15°. It may be obtained by any of the general methods, but is best prepared by the action of ethyl sulphuric acid on potassium bromide, as in the experiment.

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[1] In this book brief pharmacological statements are frequent. For full information on these points consult the excellent pharmacology text-books by *Cushny* and by *Sollmann.*

EXPERIMENT. Into a 250 c.c. flask put 55 c.c. of concentrated sulphuric acid; add quickly 55 c.c. of ethyl alcohol, shaking at the same time. Cool the flask by holding it in running water, add 38 c.c. of iced water, and cool again. Meanwhile set up a condenser having an adapter attached. Use a rapid stream of water in the condenser. Put into the flask 50 gm. of powdered potassium bromide, then place the flask on a sand bath and attach to the condenser. Fill an Erlenmeyer flask one third full of ice-water and have the adapter dip below the surface of the water. Place this receiving flask in a bath of cold water containing lumps of ice. Heat rapidly and continue heating as long as any distillate comes over. Watch that the contents of the receiver be not sucked up into the condenser. If this is threatened turn the adapter so that air can enter it.

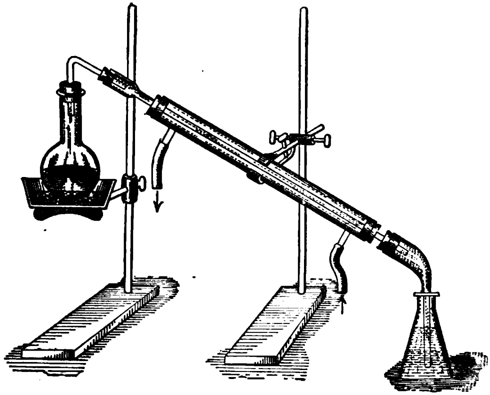

FIG. 19.

Decant most of the water from the ethyl bromide, then add ice-water and agitate. Decant the water.

Wash several times in this manner. Finally shake the washed ethyl bromide with a dilute sodium carbonate solution; do not, however, cork the flask. Transfer the bromide to a separating funnel, and run out the bottom layer into a dry flask. Add dry calcium chloride, cork tightly, and let it stand in a cool place. After a day or so distil from a small fractionating flask, using a water bath. Place an empty receiving flask in cold water. Note the boiling-point. Take the specific gravity in a small picnometer holding 5 or 10 c.c. The following equations will explain the reactions:

$$\underset{\text{(Ethyl alcohol)}}{C_2H_5OH} + H_2SO_4 = \underset{\text{(Ethyl sulphuric acid)}}{CH_3\cdot CH_2\cdot HSO_4} + H_2O,$$

$$CH_3\cdot CH_2\cdot HSO_4 + KBr = \underset{\text{(Ethyl bromide)}}{CH_3\cdot CH_2Br} + \underset{\text{(Acid potassium sulphate)}}{KHSO_4}.$$

Other halogen derivatives (besides the alkyl halides) **are** illustrated by the following compounds: dichlormethane, CH_2Cl_2; dibrommethane, CH_2Br_2; diiodomethane, CH_2I_2; trichlormethane, $CHCl_3$; tribrommethane, $CHBr_3$; triiodomethane, CHI_3; and tetrachlormethane, CCl_4.

Of the many compounds thus derived from the paraffins the three trihalogen substitution products of methane are the only ones of importance.

Chloroform (trichlormethane), $CHCl_3$, is a liquid having a pleasant odour and a sweetish taste. Its boiling-point is 61° at 731 mm. Its specific gravity is 1.498 at 15°. It is slightly soluble in water, and is a solvent for many substances. Chloroform is a very useful general anæsthetic, but is considered less safe than ether. Since it is not inflammable it can be used at night as an anæsthetic. It is not a stable compound, as exposure to light, air, and moisture causes some decomposition, thus furnishing the poisonous impurities, chlorine, hydrochloric acid, and carbon oxychloride or phosgene ($COCl_2$). These impurities can be readily detected, since chloroform containing them gives a precipitate when shaken with silver nitrate solution. Pure chloroform or other halogen substitution products do not immediately give a precipitate with silver nitrate, because they furnish no halogen ions (see p. 52). The addition of alcohol to chloroform, to the extent of one per cent, prevents decomposition. The method of its preparation is given in the following experiment. In it, chlorine (from bleaching-powder) in the presence of water oxidizes alcohol to aldehyde, then chlorine replaces hydrogen in aldehyde, giving trichloraldehyde or chloral (really chloral hydrate, see p. 107), and by the action on the chloral of the calcium hydroxide present in the mixture chloroform is produced.

EXPERIMENTS. (1) *Preparation.* Into a 2-litre flask put 300 gm. of fresh bleaching-powder, 800 c.c. of water, and 40 c.c. of alcohol, mixing well. Attach to an upright reflux condenser and heat on a water bath for one hour (an extra 20 c.c. of alcohol may be added through the condenser after 30 minutes' heating). Cool below 60°. Detach the flask and connect it with an ordinary condenser, then distil off the chloroform. Transfer the distillate to a separating funnel, shake with dilute sodium hydroxide solution, run off the bottom layer of chloroform, put the latter into the emptied funnel, add water, and shake. Run the chloroform into a dry flask, add calcium chloride, cork, and let it stand a day or so. Redistil from a fractionating flask. The following equations will explain the reaction:

$$Cl_2 + H_2O = 2HCl + O,$$

$$CH_3\cdot CH_2OH + O = CH_3\cdot CHO + H_2O,$$

$$2CH_3\cdot CHO + 3Cl_2 = 2CCl_3\cdot CHO,$$

or condensed, as follows:

$$\underset{\text{(Ethyl alcohol)}}{4CH_3\cdot CH_2OH} + \underset{\substack{\text{(Calcium}\\ \text{hypochlorite)}}}{2Ca(ClO)_2} = \underset{\text{(Aldehyde)}}{4CH_3\cdot CHO} + 2CaCl_2 + 4H_2O,$$

$$4CH_3\cdot CHO + 6Ca(ClO)_2 = \underset{\text{(Chloral)}}{4CCl_3\cdot CHO} + 6Ca(OH)_2,$$

$$2CCl_3\cdot CHO + Ca(OH)_2 = \underset{\text{(Chloroform)}}{2CHCl_3} + \underset{\text{(Calcium formate)}}{Ca(OOCH)_2}.$$

(A mixture of 30 c.c. of acetone and 70 c.c. of water could be used instead of the alcohol, this solution being added gradually from a dropping funnel to the flask containing the bleaching-powder and water.)

(2) To 1 c.c. of chloroform add half a test-tube of distilled water and shake vigorously. Remove the water with a pipette. Wash three times in this manner, testing the last wash-water with silver nitrate solution; if no precipitate appears, add silver nitrate to the washed chloroform. Let it stand, observing whether a precipitate forms later.

(3) Heat together in a test-tube 1 c.c. of chloroform, 5 c.c. of alcoholic solution of NH_3,[1] and 1 c.c. of alcoholic KOH.[2] Empty into an evaporating dish and evap-

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[1] Made by bubbling NH_3 into alcohol.

[2] To 40 c.c. of alcohol add 20 c.c. of 30% KOH.

orate almost to dryness on a water bath. Note the odour of the residue. Dissolve the residue in a few cubic centimetres of water, and test for KCN by making strongly alkaline with NaOH, then adding a few drops of $FeSO_4$ solution and one drop of Fe_2Cl_6 solution. Boil two minutes, cool, acidify with HCl; a greenish-blue colour should develop (see p. 4):

$$\begin{aligned} Cl_3\boxed{HC + N}H_3 &= HCN + 3HCl, \\ HCN + KOH &= KCN + H_2O. \end{aligned}$$

Bromoform (tribrommethane), $CHBr_3$, is a liquid which boils at 151.2°. On cooling it becomes solid, melting at 7.8°. Its specific gravity is 2.9 at 15°. It has been used as a general anæsthetic, but is unsafe.

Iodoform (triiodomethane), CHI_3, is a yellow crystalline solid, the crystals having the form of hexagonal plates. Its odour is peculiar and characteristic. It melts at 119°. It is used in surgery as an antiseptic, the action being probably due to iodine which is freed. Its method of preparation is illustrated in the following experiment:

EXPERIMENTS. (1) To 1 c.c. of alcohol in a test-tube add 10 c.c. of a strong solution of iodine in potassium iodide solution; now add, drop by drop, NaOH solution until the colour of the mixture is changed to a faint yellow. Warm the test-tube gently, noting the odour. After cooling, filter and wash the crystals. When dried in a desiccator, a melting-point determination may be made.

(2) Make a yellow solution of iodoform in alcohol,

set it aside loosely covered; by slow evaporation of the alcohol hexagonal crystals of considerable size are formed.

This reaction, besides being given by alcohol, is given by aldehyde, acetone, and other compounds which contain the group $CH_3 \cdot CO—$ (see p. 140). On account of its strong odour, the production of iodoform in this manner is often used as a test for the presence of alcohol or other substances containing the above group.

Iodoform Substitutes. Because of the unpleasant odour of iodoform many antiseptic preparations have been put on the market which disguise or eliminate the bad odour. Such are *eka-iodoform* (iodoform with paraformaldehyde), *iodoformin* (iodoform with hexamethylenetetramine), *iodoformogen* (proteid compound of iodoform), and *anozol* (iodoform and thymol). *Diiodoform* is tetraiodoethylene, C_2I_4 (see ethylene, p. 230).

Similar to the alkyl halides are the alkyl combinations with metals, as zinc methyl, $Zn(CH_3)_2$, and sodium methyl, $NaCH_3$. Both of these are important reagents.

CHAPTER IX.

ETHERS.

THE alkyl oxides are called ethers. They consist of two organic radicles linked to an oxygen atom, as methyl ether, $CH_3—O—CH_3$; ethyl ether, $C_2H_5—O—C_2H_5$.

A general method of *synthesis* is shown by the following equations:

$$CH_3 \cdot O\boxed{Na + I}CH_3 = CH_3—O—CH_3 + NaI,$$

(Sodium methylate) (Methyl iodide) (Methyl ether)

$$C_2H_5 \cdot O\boxed{Na + I}C_2H_5 = C_2H_5—O—C_2H_5 + NaI.$$

(Sodium ethylate) (Ethyl iodide) (Ethyl ether)

Methyl ether is a gas and is unimportant.

Ethyl ether is common ether. Pure ether is a liquid, boiling at 34.6° (33.6° at 734 mm. barometric pressure) and having a specific gravity of 0.718 at 15.6° and 0.731 at 4°. It dissolves to a certain extent (about 6.5 per cent) in water; it also takes up about 1¼ per cent of water. To obtain absolute ether, it is necessary to distil after the addition of metallic sodium to the ether ($Na + H_2O = NaOH + H$). It vaporizes readily, and, when rapidly evaporated, abstracts enough heat to freeze water if the latter is contained in a small vessel surrounded by the ether. The vapour is heavier than air and consequently falls. It is very inflammable, and should therefore be kept away from a flame. Ether is a solvent for a great number of substances. It is extensively used as an anæsthetic, being quite safe when properly administered. Heat is liberated when chloroform and ether are mixed in certain proportions.

Because of the use of sulphuric acid in its production, it is sometimes called sulphuric ether. To prepare it, ethyl alcohol is allowed to slowly flow into heated ethylsulphuric acid (see p. 84) contained in a flask. The following experiment will make clear how this is done.

EXPERIMENT. In a litre flask mix 165 c.c. of C.P. H_2SO_4 with 210 c.c. of alcohol. Fit a cork, pierced with three holes, into the mouth of the flask. One hole is to admit the bent tube connecting with the condenser, another holds a thermometer, and the third is for a dropping funnel which contains ethyl alcohol. The bulb of the thermometer is immersed in the liquid. When all is ready, place the flask on a sand bath and connect with the condenser. Submerge the receiving flask in a cold bath and use an adapter (*cf.* ethyl bromide, p. 83). Heat rapidly until the ethylsulphuric acid has a temperature of 140°, at which point it must be kept for the rest of the process. Run in *a very little* alcohol from the funnel. At intervals, i.e., when the amount of ether vapour diminishes, add more alcohol, a few cubic centimetres at a time. Keep flames away from the vicinity of the receiving flask. Watch the apparatus constantly. When sufficient distillate has been secured, wash it with dilute NaOH solution in a separating funnel, then with several small portions of water; draw off the water, pour the ether into a dry flask, add calcium chloride, and cork tightly. Redistil after a day or so. The following equations will explain the reaction:

$$\underset{\text{(Ethyl alcohol)}}{C_2H_5OH} + H_2SO_4 = \underset{\text{(Ethylsulphuric acid)}}{C_2H_5\cdot HSO_4} + H_2O,$$

$$C_2H_5O\boxed{H + HSO_4}\cdot C_2H_5 = \underset{\text{(Ether)}}{C_2H_5 \quad O—C_2H_5} + H_2SO_4.$$

Mixed ethers contain two different organic radicles linked to the same oxygen atom, as methyl ethyl ether, $CH_3—O—C_2H_5$. They may be formed by a synthetic process similar to that described above for simple ethers, thus:

$$CH_3\cdot O\boxed{Na + I}C_2H_5 = CH_3—O—C_2H_5 + NaI.$$

It is interesting to note that the boiling-point of methyl ethyl ether (11°) is intermediate between that of dimethyl ether, $(CH_3)_2O$ (−23.6°), and that of diethyl ether, $(C_2H_5)_2O$ (34.6°).

The ethers are very stable, not being affected by boiling with alkali or dilute acid.

CHAPTER X.

PRIMARY ALCOHOLS.

ONE of the most important classes of organic compounds are the alcohols. The empirical formula of a monacid alcohol can be derived from the formula of the paraffin hydrocarbon containing the same number of carbon atoms, by attaching an atom of oxygen, thus: $C_nH_{2n+2}O$.

Alcohols, however, are not oxides of the hydrocarbons. They are *hydroxides*. Alcohols cannot be obtained by direct oxidation of the hydrocarbons. *That the oxygen atom is present in hydroxyl* is proven by the following reactions:

(1) $$\underset{\text{(Methyl alcohol)}}{CH_3|\boxed{OH+H}|}Cl = \underset{\text{(Methyl chloride)}}{CH_3Cl} + HOH$$

$$(cf.\ K|\boxed{OH+H}|Cl = KCl + HOH),$$

(2) $$3CH_3OH + \underset{\substack{\text{(Phosphorus}\\ \text{trichloride)}}}{PCl_3} = 3CH_3Cl + \underset{\substack{\text{(Phosphorous}\\ \text{acid)}}}{P(OH)_3}$$

$$(cf.\ 3HOH + PCl_3 = 3HCl + P(OH)_3),$$

(3) $$CH_3OH + H_2SO_4 = CH_3HSO_4 + HOH$$

$$(cf.\ KOH + H_2SO_4 = KHSO_4 + HOH),$$

(4) $$CH_3OH + \underset{\text{(Acetic acid)}}{CH_3 \cdot COOH} = \underset{\text{(Methyl acetate)}}{CH_3 \cdot COO \cdot CH_3} + HOH$$

$$(cf.\ KOH + CH_3 \cdot COOH = CH_3 \cdot COOK + HOH).$$

The striking similarity between the reactions of alcohol and the most typical of all hydroxides (viz., KOH and H_2O) is clearly shown by these reactions.

The reaction of potassium and sodium with alcohols shows further that one particular hydrogen atom of the latter has a different linking from that of the other three hydrogen atoms:

$$CH_3OH + Na = \underset{\text{(Sodium methylate)}}{CH_3ONa} + H$$

$$(cf. \qquad HOH + Na = NaOH + H).$$

Finally, the structure of an alcohol is settled beyond a doubt by its *synthesis* from an alkyl halide by the action of a strong hydroxide:

$$CH_3\boxed{Cl + K}OH = CH_3OH + KCl.$$

Inorganic hydroxides are strong bases, because they furnish many hydroxyl ions when dissolved in water (see p. 124). Alcohols, on the other hand, *are not bases;* they ionize very slightly, if at all. It is to be noted that the change of one hydrogen atom of the hydrocarbon molecule into hydroxyl greatly alters the chemical behaviour of the compound; the paraffin is very stable and enters into reaction with very few reagents, whereas the alcohol is quite *reactive,* being readily affected by many reagents.

MONACID PRIMARY ALCOHOLS.

These comprise the most important group of alcohols. They form an homologous series beginning with methyl alcohol. There is a regular increase of specific gravity and boiling-point from the lowest to the highest members of the series.

Methyl alcohol (methanol, carbinol), $H \cdot CH_2OH$ or CH_3OH, is obtained from the distillate produced by the destructive distillation of wood (see p. 114). The crude alcohol is therefore called wood alcohol. It is also secured by destructive distillation of vinasse, which is the residue left after ordinary alcohol has been distilled off from fermented beet sugar molasses.

Fractional distillation does not suffice to free the methyl alcohol from the acetic acid, acetone, and other constituents of crude wood spirits.

A crystalline compound, methyl oxalate $(CH_3)_2C_2O_4$, can be formed by treatment with oxalic acid. The purified crystals can then be decomposed by boiling with ammonia water, yielding pure methyl alcohol:

$$(CH_3)_2C_2O_4 + 2NH_3 + 2H_2O = 2CH_3OH + (NH_4)_2C_2O_4.$$

The process of production of pure methyl alcohol is more difficult and expensive than is that of ethyl alcohol.

Methyl alcohol boils at 64.5°, and its specific gravity at $\frac{15.6^\circ}{15.6^\circ}$ is 0.7931 (at $\frac{0^\circ}{0^\circ}$ it is 0.812). It mixes readily with water, exhibiting the phenomena of contraction of volume and liberation of heat. It is a useful solvent; in consequence, the crude alcohol is used in the preparation of paints. It is intoxicating if taken internally; crude wood alcohol is dangerous, however, having caused many deaths when used as a substitute for ethyl alcohol. Wood alcohol burns with a blue flame, hence its use in alcohol lamps.

Ethyl alcohol (ethanol), $CH_3 \cdot CH_2OH$ or C_2H_5OH, is common alcohol. Its relation to methyl alcohol is seen when it is considered as methyl alcohol in which one hydrogen atom is replaced by the methyl radicle:

$$H \cdot CH_2OH \rightarrow CH_3 \cdot CH_2OH.$$

The name *methyl carbinol* expresses this relation. Similarly the higher alcohols are called carbinols (the prefix in each case indicating the groups attached).

Alcohol is produced by fermentation of dextrose (glucose) by means of yeast:

$$\underset{\text{(Dextrose)}}{C_6H_{12}O_6} = 2CO_2 + 2CH_3 \cdot CH_2OH.$$

About five per cent of the dextrose forms by-products, such as amyl alcohol, glycerol (i.e., glycerine), and succinic acid. Alcoholic beverages are obtained by fermentation of fruit juices containing sugar, as wine from grapes, or of malted grain, as beer from barley. Fermentation is inhibited when the alcohol content reaches about fifteen per cent. Malt liquors contain from two to eight per cent of alcohol. Wines contain eight to fifteen per cent. Stronger wines are made from these by adding alcohol. Brandy is obtained by distillation of wine, whiskey by distillation of fermented grain; both of these contain forty to sixty per cent of alcohol. Many liquors require ageing in order that the by-products which are disagreeable and injurious, as for instance fusel-oil, may be converted into ethereal compounds of pleasant taste and odour. The amount of alcohol present in a liquor can be readily estimated by distilling 100 c.c. of the liquor (diluted with 50 c.c. of water); when 100 c.c. of distillate has been collected, its specific gravity is determined. The percentage of alcohol is found by referring to tables of specific gravities (see Appendix, p. 345).

Preparation. Commercial alcohol is made from the cheapest forms of starch, potato or corn. The ground or mashed raw material is superheated with steam under pressure; then the pressure is suddenly lowered, causing the moisture within the starch granules to turn into steam and thus to rupture the granules by the explosive effect. After cooling, malt[1] is added and the mixture is kept at 60°–65°. Malt contains a ferment, *diastase*, which changes starch into the sugar maltose, and, to the extent of about 20 per cent, into dextrin. The sugar solution is diluted, and yeast is added.

The yeast furnishes a ferment which splits or inverts the maltose molecule into two dextrose molecules, and also a ferment which decomposes the dextrose into alcohol and carbon dioxide. These ferments can be extracted from the yeast cells by grinding the latter with fine quartz sand and subjecting the mass to a very high pressure (up to 300 atmospheres), and finally filtering the extract through porcelain. This filtrate contains no yeast cells, but it inverts maltose into dextrose and changes dextrose into alcohol.

The ferment in this cellular extract from yeast is called *zymase*. Similar intracellular ferments can be obtained from certain bacteria. Ferments are often called *enzymes*.

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[1] Malt is obtained by allowing barley to germinate to a certain stage.

The weak alcoholic solution (about 5 per cent) is next subjected to fractional distillation. The crude distillate is filtered through animal charcoal, which removes many impurities. It is then redistilled, the product being *ordinary alcohol* (90 to 95 per cent). This is apt to contain some aldehyde. The strongest alcohol obtainable by the most careful fractionation contains 4 per cent by weight of water and has a lower boiling-point than absolute alcohol. Commercial absolute alcohol contains about one half of one per cent of water. It is obtained by digesting alcohol with quicklime and then distilling.

$$CaO + H_2O = Ca(OH)_2.$$

More nearly absolute alcohol is secured by treating with metallic sodium and distilling.

Properties. *Chemically absolute alcohol* is almost unknown, because it takes up moisture so rapidly when exposed to the air. Absolute alcohol has a specific gravity of 0.76326 at $\frac{15^\circ}{4^\circ}$ or 0.806 at $\frac{0^\circ}{0^\circ}$, and boils at 78.3° (corrected) (at 734 mm. pressure it boils at 77.7°). It solidifies at -112°. It has much less odour than common alcohol. Alcohol burns with a colourless flame. When mixed with water, rise of temperature and contraction of volume are observed. It is an intoxicant; the detrimental effect of alcoholic liquors, however, is due *in part* to other compounds besides the alcohol. Alcohol is of great service as a solvent. *Methylated* or *denatured* alcohol is alcohol to which wood alcohol or nauseous substances have been added to render it unfit to drink. Such alcohol can be sold duty-free in many countries.

EXPERIMENT. Into a large bottle or flask put 500 c.c. of 10% glucose solution, and add some crumbled yeast. Through a cork, which tightly fits the bottle or flask, pass a glass tube which is bent so as to extend down into a small bottle containing some baryta water, the tip of the tube just reaching the surface of the latter; through a second hole in its cork the baryta bottle is connected with a tube or tower of soda-lime. Thus CO_2 cannot enter the apparatus from without. Let it stand a few days, after which a copious precipitate of $BaCO_3$ is obtained. Now distil the fermentation mixture. Apply the iodoform test to the first 10 c.c. of distillate (see p. 87). The specific gravity of the next 25 c.c. might be determined.

Experiments with 95% *alcohol.* (1) Shake 10 c.c. in a test-tube with anhydrous $CuSO_4$; the $CuSO_4$ becomes bluish (with absolute alcohol no blue colour appears). Explain what takes place.

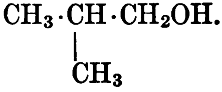
(2) Take 52 c.c. of alcohol and 48 c.c. of water, each being at a temperature of 20°, mix them in a 100 c.c. graduate, note the maximum temperature, cool to 20°, and read off the volume (about 96.3 c.c. instead of 100 c.c.).

Of other primary alcohols little need be said here.

Propyl alcohol is $CH_3 \cdot CH_2 \cdot CH_2 \cdot OH$.

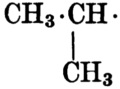
Normal butyl alcohol is $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2OH$.

Primary isobutyl alcohol is

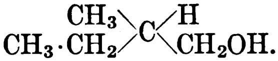


$$\underset{\displaystyle CH_3}{CH_3 \cdot \underset{|}{CH} \cdot CH_2OH.}$$

Normal amyl alcohol is $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2OH$.

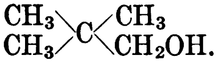


Primary isoamyl alcohol, called isobutyl carbinol, is $CH_3 \cdot \underset{\displaystyle CH_3}{\underset{|}{CH}} \cdot CH_2 \cdot CH_2OH$; this is the main constituent of *fermentation amyl alcohol.* Both of these amyl alcohols are contained in fusel-oil and in certain liquors, especially recently distilled brandy and whiskey. They are poisonous. There are three isoamyl alcohols having the same structural formula,



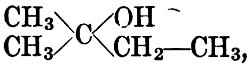
$$\begin{matrix} CH_3 \\ CH_3 \cdot CH_2 \end{matrix} > C < \begin{matrix} H \\ CH_2OH. \end{matrix}$$

Their chemical and physical properties are identical, except that their action on polarized light is different. One rotates the beam of light to the left, another rotates it to the right—these are the *active amyl alcohols;* the third does not cause rotation and is called *inactive amyl alcohol.*[1] There is also another amyl alcohol containing the primary alcohol group,



$$\begin{matrix} CH_3 \\ CH_3 \end{matrix} > C < \begin{matrix} CH_3 \\ CH_2OH. \end{matrix}$$

There is a **tertiary isoamyl alcohol,**



$$\begin{matrix} CH_3 \\ CH_3 \end{matrix} > C < \begin{matrix} OH \\ CH_2—CH_3, \end{matrix}$$

which has been used as a hypnotic under the name **amylene hydrate.**

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[1] For a discussion of this form of isomerism see p. 167.

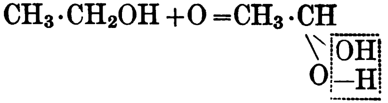
CHAPTER XI.

ALDEHYDES.

If a primary alcohol be oxidized the first product is an aldehyde:

$$CH_3 \cdot CH_2OH + O = CH_3 \cdot CHO + H_2O.$$

Two atoms of hydrogen have been removed from the alcohol molecule, hence the name *al*(*cohol*) *dehyd*(*rogenatus*). The reaction is more accurately indicated as follows:



$$CH_3 \cdot CH_2OH + O = CH_3 \cdot \underset{\diagdown\, O \boxed{\begin{array}{l}OH \\ -H\end{array}}}{CH}$$

Two hydroxyls become attached to the same carbon atom, but, as is the rule[1] in organic compounds, such a combination is too unstable to persist and H_2O splits off.

It is to be noticed that the *aldehyde group*. *—CHO contains no hydroxyl.* This can be proven experimentally. If alcohol or any other hydroxyl-containing compound be treated with phosphorus pentachloride, the place of each hydroxyl group is taken by a chlorine atom and hydrochloric acid is a by-product of the reaction:

$$CH_3 \cdot CH_2OH + PCl_5 = CH_3 \cdot CH_2Cl + POCl_3 + HCl.$$

---

[1] There are three well-known exceptions to this rule, in the case of chloral hydrate, mesoxalic and glyoxylic acid.

But if an aldehyde be similarly treated a dichlor-compound is obtained and no hydrochloric acid:

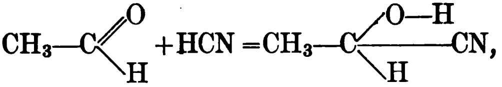
$$CH_3 \cdot CHO + PCl_5 = CH_3 \cdot CHCl_2 + POCl_3.$$

Therefore the aldehyde group must be written CHO, not COH.

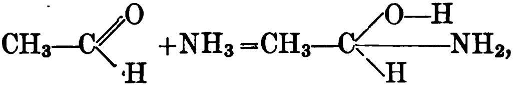
All aldehydes are strong reducing agents, because they readily take up oxygen to form acids. The common tests for sugar are really aldehyde reactions, as practically all sugars contain the CHO group. The reduction of silver and copper salts is illustrated by the experiment below.

The aldehydes are named from the acids which they produce when oxidized: thus, H·CHO is formic aldehyde or formaldehyde, and CH_3·CHO is acetic aldehyde or acetaldehyde.

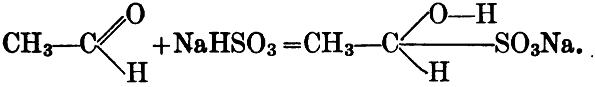
The linking C═O in the aldehyde group causes aldehydes to act like unsaturated compounds, for they readily form addition compounds, thus:



(Acetaldehyde) (Acetaldehyde cyanhydrin)



(Aldehyde ammonia)

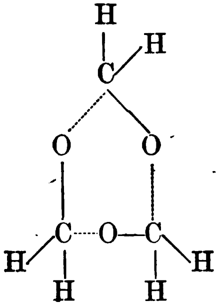


(Sodium acid sulphite) (Aldehyde bisulphite)

Aldehydes (except chloral hydrate) cause a violet-red colour to appear when added to a solution of fuchsin which has been decolorized by sulphurous acid. This reaction is due to the formation of condensation products (see acetaldehyde). Nascent hydrogen converts an aldehyde into the corresponding primary alcohol.

Formaldehyde (methanal), H·CHO, is a gas. It is quite soluble in water. Commercial *formalin* is a 40 per cent solution. Formaldehyde may be prepared by bubbling air through methyl alcohol which is kept at about 50°; then the mixture of air and vapour is passed through a heated tube containing a copper or platinum spiral: $H \cdot CH_2OH + O = H \cdot CHO + H_2O$. It is also produced by burning methyl alcohol in a special lamp in which the supply of air is limited so that incomplete combustion occurs; part of the alcohol is oxidized to formaldehyde and escapes. This lamp can be used for disinfection of rooms.

Formaldehyde has a tendency to form polymers. A polymer has a molecular weight which is an even multiple of that of the original substance, and it has the same percentage composition as the latter (see p. 57). Thus **paraformaldehyde** is $(H \cdot CHO)_n$. The graphic representation of $(H \cdot CHO)_3$ would be



Paraformaldehyde (paraform) is a white crystalline substance, which, on being heated, is converted into formaldehyde. It is sold in the form of tablets or candles for disinfecting purposes.

Formaldehyde is an efficient germicide, and is therefore used extensively for disinfecting purposes. It is used either as the gas or in dilute solution. It is very irritating to the eyes and mucous membranes. The dilute solution also hardens albuminous substances, and is consequently used to prepare tissues for histological examination. It converts a solution of gelatin into a hard insoluble mass.

EXPERIMENTS. (1) To a few cubic centimetres of concentrated H_2SO_4 in a test-tube add a few drops of ferric chloride solution; with a pipette run in about 5 c.c. of dilute formaldehyde solution as a top layer, avoiding mixing with the H_2SO_4—a violet zone between the two layers forms, quickly disappearing.

(2) Set in a desiccator an evaporating dish containing 10 c.c. of formalin. Leave several days until a white solid, paraformaldehyde, is obtained. When this is secured, heat some of it in a dry test-tube. It volatilizes completely, passing away as formaldehyde gas. Note the odour. Be careful not to get strong fumes into the eyes or nostrils, as the gas is very irritating.

(3) Dissolve 3 gm. of gelatin in 100 c.c. of water; add 2 c.c. of commercial formalin. The fluid becomes solid an insoluble compound of gelatin being formed.

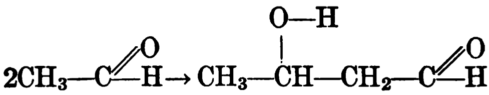
(4) In a water bath kept at about 20°, place a large evaporating dish containing 60 c.c. of milk to which a little formaldehyde has been added. Float on the

milk a watch-glass containing about 1 c.c. of a fresh solution of 0.35% of morphine sulphate in C.P. H_2SO_4. Cover the evaporating dish with a glass plate. Note the time it takes to secure a purple margin or general coloration of the acid. Repeat with diluted milk. This has been proposed as a method of approximate quantitative estimation, for it is claimed that if the colour appears in fifteen minutes, the milk contains about 1 part in 2500, if in forty-five minutes 1 part in 15000, if in sixty minutes 1 part in 25000. The acid solution of morphine must be kept away from formaldehyde vapours and the solution should be freshly prepared.

Acetaldehyde (ethanal, aldehyde), $CH_3 \cdot CHO$, can be obtained in similar manner as formaldehyde by the oxidation of ethyl alcohol vapour, induced by heated platinum. The oxidation is generally effected, however, by the use of sulphuric acid and sodium or potassium dichromate as described in the experiment below. Acetaldehyde boils at 20.8° and has a specific gravity of 0.780 at 20°.

Acetaldehyde can be changed into the polymers, **paraldehyde,** a liquid boiling at 125°, and **metaldehyde,** a solid. Both have the formula $(CH_3 \cdot CHO)_3$. Paraldehyde is a hypnotic.

Aldehyde molecules can be made to fuse together, forming a "condensation" product, *aldol.* Zinc chloride will effect this change:



$$2CH_3—\overset{O}{\overset{\|}{C}}—H \rightarrow CH_3—\overset{O—H}{\overset{|}{CH}}—CH_2—\overset{O}{\overset{\|}{C}}—H$$

It has been suggested that the production of starch and sugar by plants may be a process of condensation of formaldehyde, the latter being synthesized from CO_2 and H_2O. A sugar can be made from formaldehyde by condensation under the influence of lime-water (see p. 213).

EXPERIMENTS. *Preparation.* (1) Mix in a large flask 100 c.c. of water and 30 c.c. of C.P. H_2SO_4. Fit a cork having two holes, one for the bent tube connecting with a condenser, the other for a dropping funnel. Have the tip of the dropping funnel about 3 cm. above the liquid. Connect with the condenser, and place the receiving flask in ice-water. Heat the flask over wire gauze to the boiling-point. Now add through the funnel, in a slow stream, a solution of sodium dichromate, containing 100 gm. of dichromate, 100 c.c. of water, and 53 c.c. of alcohol. Remove the flame as soon as distillation is well started. If vapour passes through uncondensed, slacken the stream. If aldehyde ceases distilling, heat again with the flame. When all of the solution has been added, redistil the distillate. Save a portion of the crude distillate for making the aldehyde tests given

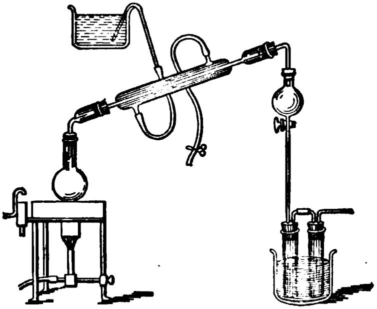
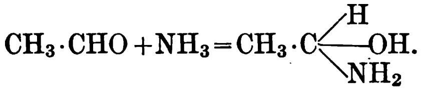


FIG. 20.

below. In redistilling tilt the condenser upward, as shown in the diagram. Circulate through it water heated to 30°, using a reservoir or large funnel. Connect the condenser with a dropping funnel, which dips into the ether in the first wash-bottle. Put 25 c.c. of dry ether into each wash-bottle. The aldehyde will not condense at 30°, while alcohol and water will, so that only aldehyde passes into the ether, which absorbs it. Keep the ether bottles in a bath of ice-water. When the aldehyde seems to have all passed over, transfer the ether to a beaker which is placed in a freezing-mixture. Now bubble into it ammonia (secured by heating NH_4OH in a flask), which has been dried by passing through a tower of soda-lime, until the odour of ammonia becomes strong. A mass of white crystals of aldehyde ammonia will appear. Filter, wash the crystals with ether, and dry in a $CaCl_2$ desiccator. From this product pure aldehyde may be obtained by dissolving some of it in an equal weight of water, adding 3½ times as much 50% H_2SO_4, and then distilling.

$$Na_2Cr_2O_7 + 4H_2SO_4 = 3O + Cr_2(SO_4)_3 + Na_2SO_4 + 4H_2O,$$

$$CH_3 \cdot CH_2OH + O = CH_3 \cdot CHO + H_2O,$$



$$CH_3 \cdot CHO + NH_3 = CH_3 \cdot C \begin{cases} H \\ OH. \\ NH_2 \end{cases}$$

(2) *Aldehyde tests.* (*a*) Add a little of the crude distillate to 5 c.c. of dilute Fehling's solution in a test-tube; boil until Cu_2O is precipitated.

(*b*) Add another small portion to a few cubic centimetres of ammoniacal $AgNO_3$ solution in a perfectly clean test-tube; heat gradually—a mirror of silver is deposited.

(*c*) To 1 c.c. of dilute rosaniline (fuchsin) solution add a solution of sulphurous acid until decolorized. Add some aldehyde solution and shake—a violet-red colour appears.

Chloral (trichloraldehyde), $CCl_3\cdot CHO$, is a chlorine derivative of acetaldehyde. It is produced by passing dried chlorine gas into absolute alcohol for several days. Aldehyde and HCl are the first products of the chlorination. The final products are chiefly chloral hydrate and chloral alcoholate, $CCl_3\cdot CH\langle\begin{smallmatrix}OH\\OH\end{smallmatrix}$ and $CCl_3\cdot CH\langle\begin{smallmatrix}OC_2H_5\\OH\end{smallmatrix}$ respectively. Chloral is liberated from these by the action of concentrated sulphuric acid.

Chloral is an oily liquid, boiling at 97.7° and having a specific gravity of 1.512 at 20°. It gives the aldehyde reactions. When it comes into contact with water it forms chloral hydrate crystals.

Chloral hydrate, $CCl_3\cdot C\begin{smallmatrix}\diagup H\\ \text{—}OH\\ \diagdown OH\end{smallmatrix}$, is believed to have two hydroxyls attached to the same carbon atom, contrary to the general rule. One reason for believing that a typical CHO group is not contained in it is the fact that it does not give the fuchsin test.

Chloral hydrate is extremely valuable as a medicine, being used as a hypnotic. It is very soluble in water and in alcohol. It melts at 57°. Alkaline solutions decompose both chloral and chloral hydrate to chloroform and formic acid:

$$CCl_3\cdot CHO + KOH = CCl_3H + \underset{\text{(Potassium formate)}}{HCOOK}.$$

Experiments. (1) Try the aldehyde tests (see acetaldehyde) with a solution of chloral hydrate.

(2) Warm a few cubic centimetres of chloral hydrate solution; after adding NaOH, notice the odour of chloroform.

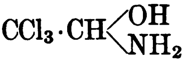
(3) Boil a few cubic centimetres of chloral hydrate solution; test part of it with $AgNO_3$—it gives no precipitate. Now add some zinc powder to the original solution and boil two minutes. Filter; test filtrate with $AgNO_3$—it gives a white precipitate of AgCl. The zinc decomposes water; the nascent hydrogen produced takes chlorine from the chloral hydrate, forming HCl (which combines with the zinc).

(4) To some dry chloral hydrate add C.P. H_2SO_4 and cool—oily drops of chloral float on the acid.

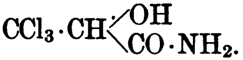
Chloral Substitutes. Many derivatives of chloral have been synthesized with the object of correcting the tendency which chloral hydrate has to depress the circulation. Such are:

Butyl-chloral hydrate (croton chloral),

$$CH_3 \cdot CHCl \cdot CCl_2 \cdot CH(OH)_2.$$

Chloralamide, 

$$CCl_3 \cdot CH\langle\begin{smallmatrix}OH\\NH_2\end{smallmatrix}$$

Chloralformamide, 

$$CCl_3 \cdot CH\langle\begin{smallmatrix}OH\\CO \cdot NH_2.\end{smallmatrix}$$

Chloralose (chloral + glucose), $C_8H_{11}Cl_3O_6$.

Hypnal (chloral + antipyrin).

CHAPTER XII.

FATTY ACIDS AND ETHEREAL SALTS. FURTHER OBSERVATIONS IN PHYSICAL CHEMISTRY.

ACIDS.

Acids are defined as substances which when dissolved in water dissociate in such a way as to furnish hydrogen ions (see p. 52). In organic chemistry all substances containing the carboxyl group, COOH, are acids. Most organic acids dissociate but feebly; they are therefore weak acids as compared with inorganic acids (see p. 123).

A general method of production of acids is by *hydrolysis*[1] of a cyanide (see experiment under acetic acid):

$$HCN + 2H_2O = \underset{\text{(Ammonium formate)}}{H \cdot COONH_4},$$

$$CH_3CN + 2H_2O = \underset{\text{(Ammonium acetate)}}{CH_3 \cdot COONH_4}.$$

The acids to be studied at this point are called **fatty acids,** because common fats contain some members of this series of acids (in combination with glycerol). They are monobasic, i.e., they contain only one displaceable hydrogen atom in the acid group. They are the end products of the oxidation of primary monacid alcohols, since they can be obtained by oxidation of aldehydes:

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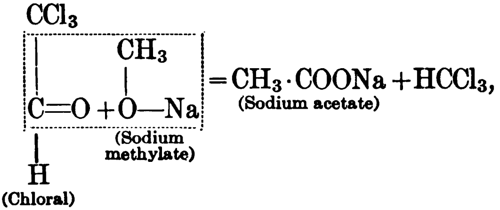
[1] Hydrolysis means introducing H_2O into the molecule of the substance to be hydrolyzed.

$$H\cdot CHO + O = H\cdot COOH.$$

The OH of carboxyl can be proven to be hydroxyl by the reaction with PCl_3 (see pp. 92 and 100), thus:

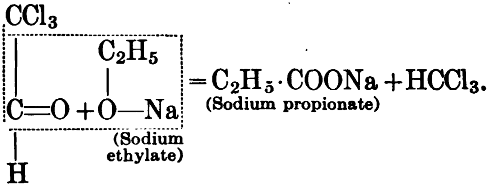
$$3CH_3\cdot COOH + 2PCl_3 = 3CH_3\cdot COCl + P_2O_3 + 3HCl.$$

The successive acids of 'the series can be built up by taking advantage of the reaction indicated in the following equations:



$$\underset{H}{\overset{CCl_3}{C}}{=}O + \overset{CH_3}{O}{-}Na = CH_3\cdot COONa + HCCl_3,$$

(Chloral) (Sodium methylate) (Sodium acetate)



$$\underset{H}{\overset{CCl_3}{C}}{=}O + \overset{C_2H_5}{O}{-}Na = C_2H_5\cdot COONa + HCCl_3.$$

(Sodium ethylate) (Sodium propionate)

Formic acid (methanoic acid), $H\cdot COOH$, is a liquid. (1) It can be made by oxidation of formaldehyde by hydrogen peroxide in alkaline solution (see exp.):

$$H\cdot CHO + H_2O_2 + KOH = H\cdot COOK + 2H_2O.$$

The acid can then be liberated from the potassium formate.

(2) Moist CO is absorbed by soda-lime at 190°–220°, forming sodium formate:

$$CO + NaOH = H \cdot COONa$$

(3) Moist CO_2 coming in contact with metallic potassium forms potassium formate and potassium bicarbonate:

$$2K + 2CO_2 + H_2O = HCOOK + KHCO_3.$$

(4) Oxalic acid when heated with glycerol (glycerine) decomposes to formic acid and carbon dioxide (see exp.).

Formic acid occurs in red ants, in stinging nettles, and in the stinging apparatus of bees. It is very irritant, causing blisters when applied to the skin. Formic acid boils at 101°; it solidifies at a low temperature and melts at 8.52°. Its specific gravity is 1.231 at 10°. It is a strong reducing agent, reducing silver and mercury compounds to the metal (see exp.). It is a stronger acid than acetic acid. When treated with concentrated sulphuric acid it is decomposed, with evolution of carbon monoxide (see exp.).

EXPERIMENTS. (1) To 0.5 c.c. of commercial formaline in a beaker add 10 c.c. of 8% NaOH (twice normal solution). Add hydrogen peroxide as long as effervescence continues and until no odour of formaldehyde remains. Titrate the solution with $\frac{N}{1}$ H_2SO_4 in the following manner: After putting a drop of methyl orange into the solution, run in the acid from a burette gradually, until the mixture remains slightly pink after stirring well. Deduct the number of cubic centimetres of H_2SO_4 from 20 c.c. (which would be neutralized by 10 c.c. of 8% NaOH); the difference indicates the amount of formic acid which has been produced. This method can be used for quantitative estimation of formaldehyde.

(2) Prepare formic acid also as follows: Into a half-litre flask put 200 c.c. of anhydrous glycerol (which has been heated at 170° for an hour); add 100 gm. of crystallized oxalic acid. Heat gradually on a sand bath. Connect with a condenser. Carbon dioxide is evolved and formic acid begins to distil at about 115° (temperature of the liquid). When the distillate ceases to come over, add 50 gm. of oxalic acid. Heat again; the heating may have to be pushed in order to get a proper amount of distillate. Repeat the addition of oxalic acid until enough distillate has been collected. (To secure all the formic acid distillation with steam (see p. 14) may be resorted to.) Test some of the acid distillate for formic acid as below. If less than 200 c.c. of distillate is obtained, dilute it. Add to it copper hydroxide which has been freshly precipitated (with NaOH) and washed, meantime warming the mixture. When copper hydroxide no longer dissolves, filter and evaporate the filtrate to a bulk of about 10 c.c. On cooling beautiful crystals of copper formate are formed:

$$\underset{\text{(Glycerol)}}{C_3H_5(OH)_3} + \underset{\text{(Oxalic acid)}}{(COOH)_2} = \underset{\text{(Monoformin)}}{C_3H_5(OH)_2OCOH} + H_2O + CO_2,$$

$$C_3H_5(OH)_2OCOH + H_2O = \underset{\text{(Formic acid)}}{H \cdot COOH} + \underset{\text{(Glycerol)}}{C_3H_5(OH)_3}.$$

(3) Test for formic acid in the distillate as follows: Warm to 50°, add HgO, and shake vigorously. Filter and boil the filtrate one minute; a gray precipitate of mercury develops:

$$HgO + H \cdot COOH = Hg + CO_2 + H_2O.$$

(4) Into a test-tube put 3 c.c. of formic acid; add slowly 6 c.c. of H_2SO_4. Cork quickly with a cork through which passes a bent delivery-tube the end of which is to dip into a few cubic centimetres of dilute hæmoglobin solution in another test-tube. The hæmoglobin is changed to carbon-monoxide-hæmoglobin, which has a cherry-red tint. The hæmoglobin solution is made by adding a drop of blood to a little distilled water.

Acetic acid, CH_3COOH. There are various ways by which ethyl alcohol may be oxidized to yield acetic acid. In the laboratory, the addition of spongy platinum to alcohol contained in an open vessel causes the atmospheric oxygen to attack the alcohol, oxidizing it and producing acetic acid. The spongy platinum itself undergoes no change; it is a *catalytic* agent, merely transferring the oxygen to the alcohol.

Pure alcohol or alcohol diluted with pure water does not spontaneously become converted into acetic acid when exposed to the air, but does so if the dilute alcoholic solution contains nitrogenous matter. This is because of the growth in the latter solution of a microörganism derived from the air (*Mycoderma aceti*), which, like spongy platinum, transfers atmospheric oxygen to the alcohol. Nitrogenous matter is necessary for the life of this organism. It is in this way that wine becomes converted into vinegar. Mere exposure of wine or cider to air would, however, occupy too much time to produce sufficient vinegar to meet the demands of commerce, and consequently the above process has to be accelerated. This is done by allowing the wine to slowly percolate through freely perforated barrels filled with beech shavings previously sown with the mycoderma by soaking them in strong vinegar. A slight amount of heat is generated during the oxidation; this creates currents of air which enter the barrels through the perforations in their sides, and in this way a sufficiency of oxygen for the process is supplied. Other alcoholic solutions besides wine may be used for the purpose, e.g., cider or beer, and frequently some alcohol obtained by fermenting glucose is added to these. The amount of alcohol in such solutions should not, however, be over ten per cent. The resulting vinegars contain about five per cent of acetic acid, besides various aromatic bodies.

To obtain acetic acid in a pure state, fermentation of alcoholic liquids is, however, not employed. For this purpose wood is subjected to what is known as *destructive distillation*. It is heated at low temperature (200°) in a retort from which air is excluded, and the vapours condensed. The resulting distillate consists of a mixture of a tarry material and a watery liquid known as pyroligneous acid. This latter contains, besides acetic acid, various other organic substances, particularly acetone and methyl alcohol. By fractional distillation several of these are separated, the second fraction, which contains most of the acetic acid, being neutralized with sodium carbonate and evaporated; the resulting sodium acetate is then dried and treated with sulphuric acid so as to liberate the acetic acid, which is then distilled. This first distillate contains about 36 per cent of acetic acid. To further purify it, this dilute acid is passed through charcoal, and then redistilled. The final distillate, however, still contains water. To separate this, the solution is cooled down to a low temperature, when most of the acid solidifies. Since pure acetic acid solidifies on cooling, it is often called *glacial acetic acid.*

Acetic acid is a colourless liquid, boiling at 118.1° (corrected) and with a specific gravity of 1.055 at 15°. By dilution with water the specific gravity rises, attaining the maximum when an acid of 80% is obtained (see table in Appendix, p. 351). When cooled down it solidifies, the crystals again melting at 16.75°. On the skin it raises blisters and causes pain. It has a characteristic odour and, in dilute solution, a pleasant acid taste.

EXPERIMENTS. (1) Into a small fractionating flask put 6 gm. of potassium dichromate and 10 c.c. of concentrated H_2SO_4; connect with a condenser; then, by means of a dropping funnel suspended by the cork of the flask, add drop by drop 12 c.c. of 20% alcohol. Heat until enough distillate is secured for the following tests.

(2) *Acetic acid tests.* (*a*) To 5 c.c. of the solution add 1 c.c. of H_2SO_4 and a few drops of alcohol. Shake, and note the odour of ethyl acetate on warming.

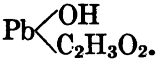
(*b*) Neutralize 5 c.c. with sodium carbonate solution. When neutral add a few drops of ferric chloride solution. The mixture becomes brownish red; on boiling a coloured precipitate separates out. Filter; the filtrate is colourless.

(3) Cool some glacial acetic acid in a large test-tube by means of ice-water, stirring with a thermometer. Melt the crystals with the heat of the hand, keeping the thermometer in motion, note the temperature at which the acid melts.

In all its reactions acetic acid conforms with the structural formula CH_3COOH. Since, in our practical exercises, we shall perform nearly all the reactions which have enabled chemists to ascribe this formula to acetic acid, it may be advantageous, when describing these reactions, to indicate how they bear out the structural formula. To illustrate clearly just exactly *how a structural formula is arrived at* by the chemist let us suppose that we are working with an unknown substance which, by elementary analysis and molecular weight determination (see Chapter III and p. 56), we have found to possess the empirical formula $C_2H_4O_2$.

In testing the reaction of this substance we shall have found it acid, and on neutralizing it with monacid bases and evaporating, crystalline salts will be obtained which on analysis will be found to contain one H atom less than the acid itself. These facts indicate that the acid dissociates into a kation of hydrogen, $H^{\cdot}$, and an anion represented by the remainder of the molecule, $C_2H_3O_2'$. In other words, one of the four H atoms must be represented in the structural formula as different from the others: $C_2H_3O_2$—H.

The bases which may be employed to neutralize the acid are conveniently divided into metallic and ethereal.

Metallic salts of acetic acid—the acetates—are very numerous. *Sodium and potassium acetates* ($C_2H_3O_2K$; $C_2H_3O_2Na$) are extensively used for various purposes in the laboratory. *Lead acetate,* $Pb(C_2H_3O_2)_2$, on account of its possessing a peculiar sweetish taste, is known as sugar of lead. It is used in medicine as an astringent. When it is mixed with lead oxide the compound is known as *basic lead acetate,*  $Pb\langle\begin{matrix}OH\\C_2H_3O_2\end{matrix}$. In the presence of carbonic acid, basic lead acetate forms densely opalescent solutions on account of the insoluble lead carbonate which is formed. In boiled distilled water the solutions are nearly clear. The lead acetates are valuable precipitating reagents and are extensively employed for this purpose in bio-chemistry. *Copper acetate* is a well-known salt and is used as a reagent. All these acetates are most simply prepared by dissolving the metallic hydroxides in acetic acid.

Ethereal Salts of Acetic Acid. In studying alcohol we saw that its hydroxyl group (OH) is replaceable, for example, by halogens (Cl, Br, or I), or, as in the case of ethereal salts, by the organic acid radicle $C_2H_3O_2$. Since the ethereal salts are of considerable importance and are numerous, we shall postpone their consideration till later.

So far we have seen that one of the H atoms in acetic acid differs considerably from the others. By another set of reactions we can show that this same H atom must be intimately connected with one of the O atoms, the resulting group, which we have already met with in alcohols, being hydroxyl. This hydroxyl is, as we have seen, replaceable by halogens. Thus, when acetic acid is treated with PCl_3, the following reaction ensues: $3C_2H_3O_2H + 2PCl_3 = 3C_2H_3OCl + 3HCl + P_2O_3$. The hydroxyl group is evidently substituted by Cl, just as in the case of water or alcohol:

$$3HOH + PCl_3 = 3HCl + P(OH)_3.$$

We must therefore assume that acetic acid can under certain conditions be caused to split up into C_2H_3O and OH. The former of these is called the *acetyl group*, the latter is of course hydroxyl.

Acetyl chloride, C_2H_3OCl, belongs to the class of *acid chlorides* and may be prepared by the method described in the following experiment:

EXPERIMENT. Put 25 c.c. of glacial acetic acid into a fractionating flask. Suspend a dropping funnel by the cork. Attach the flask to a condenser. As a receiver, fit a filtering flask on to the condenser-tube with a cork (see fig. 21), and attach to the side tube of the filtering flask a calcium chloride tube. All moisture must be carefully excluded in this manner. Add to the acid through the dropping funnel 20 gm. of phosphorus trichloride, the flask being immersed in a bath of ice-water. When cooled, substitute a warm bath at 40°–50°. Keep the temperature at this point until the evolution of HCl ceases (have the apparatus under a hood). Bring the water of the bath to active boiling and distil the acetyl chloride.

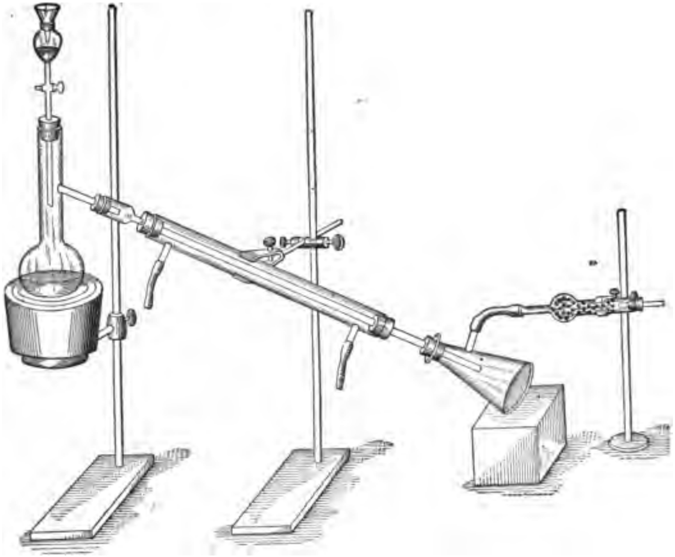


FIG. 21.

It is a colourless volatile fluid, boiling at 55°. In the presence of water it readily decomposes, as represented in the following equation:

$$C_2H_3O\boxed{Cl+H}OH = C_2H_3OOH + HCl.$$

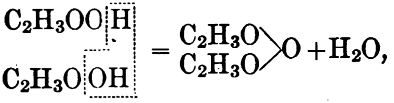
The atmospheric moisture is sufficient to cause this reaction, so that when acetyl chloride is exposed to the air it fumes, the fumes being very suffocating and disagreeable. (It should be kept in tightly stoppered bottles.) The H of the hydroxyl group of alcohols reacts similarly with acetyl chloride, thus:

$$C_2H_3O\boxed{Cl+H}OC_2H_5 = \underset{\textbf{(Ethyl acetate)}}{C_2H_3OOC_2H_5} + HCl,$$

the ethereal salt of acetic acid with the radicle of the alcohol used being formed. On this account acetyl chloride is an invaluable reagent for the detection of hydroxyl; if we find that a substance when treated with acetyl chloride forms an ethereal acetate we may conclude that the substance contains hydroxyl other than the hydroxyl of carboxyl.

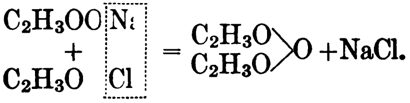
Experiment. To 3 c.c. of absolute alcohol add 3 c.c. of acetyl chloride. HCl is evolved. Note the odour of ethyl acetate.

The above experiments, therefore, justify our writing the formula C_2H_3OOH. Further corroboration of this is found in the fact that two molecules of acetic acid can be made to unite together with the loss of a molecule of water, thus:



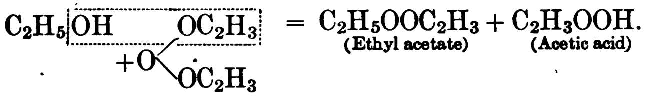
$$\begin{array}{l} C_2H_3OO\,H \\ C_2H_3O\,OH \end{array} = \begin{array}{l} C_2H_3O \\ C_2H_3O \end{array}\!\!> O + H_2O,$$

the resulting body being **acetic anhydride.** For practical purposes acetic anhydride may be prepared by acting on acetyl chloride with anhydrous sodium acetate, thus:



$$\begin{array}{c} C_2H_3OO\,Na \\ + \\ C_2H_3O\quad Cl \end{array} = \begin{array}{l} C_2H_3O \\ C_2H_3O \end{array}\!\!> O + NaCl.$$

It is a fluid giving off a suffocating vapour. Added to water, it sinks to the bottom of the vessel, but gradually becomes reconverted into acetic acid. Its readiness to re-form acetic acid causes it to attack the hydroxyl group of alcohols and other hydroxyl compounds, one of the acetyl groups becoming thereby attached in place of the OH group, thus:



$$C_2H_5OH + O\begin{matrix}OC_2H_3\\OC_2H_3\end{matrix} = \underset{\text{(Ethyl acetate)}}{C_2H_5OOC_2H_3} + \underset{\text{(Acetic acid)}}{C_2H_3OOH}.$$

Like acetyl chloride, it may therefore be employed for ascertaining whether a substance contains hydroxy not in carboxyl, and if so, how many such groups it contains (see p. 151).

There remains for us to find out *how the acetyl radicle C_2H_3O is composed.* A clue to this is furnished by the observation that methane, CH_4, and a carbonate are obtained by heating anhydrous sodium acetate with soda-lime (see exp., p. 77):

$$C_2H_3OONa + NaOH = Na_2CO_3 + CH_4.$$

This must mean that the two carbon atoms are of different value and that one of them exists in combination with hydrogen as methyl, CH_3.

Further corroboration of this is furnished by the fact that acetic acid can be produced by the hydrolysis of methyl cyanide[1] (see exp.), thus:

$$CH_3CN + 2H_2O = CH_3COOH + NH_3,$$

and also by the fact that the three H atoms which belong to the methyl group can be separately replaced by chlorine atoms, thus forming the substitution products *mono-, di-, or tri-chloracetic acid:*

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[1] Methyl cyanide may be obtained by methods described on p. 155.

$$C_2H_3O \cdot OH + Cl_2 = C_2H_2ClO \cdot OH + HCl,$$
$$C_2H_2ClO \cdot OH + Cl_2 = C_2HCl_2O \cdot OH + HCl,$$
$$C_2HCl_2O \cdot OH + Cl_2 = C_2Cl_3O \cdot OH + HCl.$$

The resulting substitution products retain the acid properties of acetic acid, such as the power of forming ethereal salts, anhydrides, etc.

If we represent acetic acid as containing a methyl group its formula must be written either CCH_3OOH or CH_3COOH: which of these is correct? A little consideration will show us that the first formula is impossible, at least in a saturated compound, so that by exclusion we must accept the latter. *Further evidence that the group COOH does actually exist in acetic acid* is given by the following observations:

(*a*) The result of the hydrolysis of methyl cyanide:

$$CH_3CN + 2H_2O = CH_3COOH + NH_3.$$

(*b*) The result of electrolysis of acetic acid. The kation $H^{\cdot}$ is liberated at the kathode; the anion CH_3COO' passes to the anode, where it is liberated as CO_2 and ethane (the two methyl (CH_3) groups from two molecules having united together).

(*c*) The formation of sodium acetate by treating sodium methyl with CO_2: $CH_3Na + CO_2 = CH_3COONa$.

EXPERIMENT. Take 2 gm. of acetonitrile (prepared as directed in the experiment under methyl cyanide, see p. 155) and mix with 10 c.c. of 60% KOH in a small flask. Attach the flask to an upright (reflux) condenser. Heat for forty-five minutes. Note the ammonia escaping from the top of the condenser. Neutralize the resulting fluid with HCl and test for acetic acid (see previous experiments):

$$CH_3CN + 2H_2O = CH_3 \cdot COONH_4,$$
$$CH_3 \cdot COONH_4 + KOH = CH_3 \cdot COOK + NH_3 + H_2O.$$

THE CAUSE OF THE RELATIVE STRENGTHS OF ACIDS (AND BASES).

It is important to understand what it is that constitutes the strength of an acid or alkali. This obviously cannot be gauged by titration with indicators: a normal solution of *any* acid will be neutralized by an equal volume of a normal solution of any alkali, and yet such acids as HCl, H_2SO_4, etc., are far more *reactive*—are stronger, in other words—than such acids as acetic, lactic, etc. This difference in strength is explained by the fact that only a certain fraction of any acid or alkali is effective, the value of this fraction being proportional to the strength of the acid or alkali. The effective fraction of an acid is that portion of it which becomes ionized. In solution, acids ionize into a kation of hydrogen (which being charged with + electricity is often called the positive ion) and an anion of the rest of the molecule (see p. 52). In the case of solutions of strong acids a much greater proportion of acid ionizes in this way than in the case of an equimolecular solution of weak acids. We may therefore state that the *active acidity of a solution of an acid depends on the concentration of the hydrogen ions.*

In the case of bases, e.g., KOH, NH_4OH, dissociation in solution into kations of the metal or its equivalent (K, NH_4) and into anions of hydroxyl occurs. It is the concentration of the *hydroxyl ions* which determines their strength (cf. amines, p. 159).

In a solution of HCl, for example, there exist: (*a*) undissociated HCl, (*b*) kations of $H^{\cdot}$, and (*c*) anions of Cl'; in a solution of acetic acid: (*a*) undissociated $CH_3 \cdot COOH$, (*b*) kations of $H^{\cdot}$, and (*c*) anions of CH_3COO': but the amount of (*a*) in the two cases will be very different, there being much less dissociation (i.e., (*a*) is of greater value) in the case of acetic acid than in the case of hydrochloric acid. In every acid, therefore, there must exist a certain proportion between the undissociated and the dissociated portions. This will, of course, vary at different dilutions, for it will be remembered that dissociation increases with dilution (see p. 53). Since it is known that the electrical conductivity of a solution depends on the amount of dissociation of the electrolyte dissolved in it, we may obtain a value for this proportion by measurement of electrical conductivity.

At infinite dilution strong acids or bases and salts are entirely dissociated; therefore at finite dilution the degree of dissociation (or the proportion of the substance existing in the state of ions) is equal to the quotient of the molecular conductivity at the dilution considered U_v, by the molecular conductivity at infinite dilution U_∞. Representing the degree of dissociation by M, we have $M = \frac{U_v}{U_\infty}$. M, therefore, expresses the strength of the acid at the dilution and temperature considered.

But it would obviously be much more convenient to possess a value which expresses the strength of the acid (or base) at *all* dilutions. Such a constant value, called k, can be obtained at least for weak acids and bases (half electrolytes, i.e., those with which we have mainly to do in organic chemistry) by Ostwald's equation $\frac{M^2}{(1-M)_v}=k$, where v represents the volume in litres containing one gram-molecule of the acid or base. As k is a small number, it is usual to multiply it by 100; the product being denoted by K.

For the more common acids K is as follows:

Formic, 0.0214; *Acetic*, 0.0018; *Propionic*, 0.0013; *n-Butyric*, 0.0015; *Valeric*, 0.0016.

It will be noted that formic is by far the strongest of these. Unfortunately for comparative purposes, strong mineral acids do not obey the law on which Ostwald's formula is based, so that we cannot obtain K for them. If, however, we take the value of M when $v=16$, we get the following comparative figures:

HCl, $100M=95.55$. Acetic acid, $100M=1.673$.

ETHEREAL SALTS.

Comparable with the salts of inorganic chemistry there are derivatives of organic acids in which the hydrogen of carboxyl is replaced by some hydrocarbon radicle. Thus ethyl acetate has the formula $CH_3COO \cdot C_2H_5$, from which it is seen that the two constituent radicles are linked together through an oxygen atom as in the ethers (see p. 89). On this account such compounds are usually called *ethereal salts* or more briefly *esters*. In a looser sense, compounds of mineral acids with organic radicles, as ethyl nitrate, $C_2H_5ONO_2$, and ethyl sulphate, $(C_2H_5)_2SO_4$, are included in this group; but since such as these have been considered elsewhere we shall study at present only those salts in which both basic and acid portions are organic.

Inorganic salts are immediately formed when solutions of an acid and a base are mixed together, for, both of these being ionized, the hydrogen ion of the acid immediately unites with the hydroxyl ion of the base to form water:

$$\underset{\text{(Base)}}{(B^{\cdot}+OH')}+\underset{\text{(Acid)}}{(H^{\cdot}+Z')}=\underset{\text{(Salt)}}{(B^{\cdot}+Z')}+H_2O.^1$$

Ethereal salts are, however, not thus readily formed, for the reacting base, being an alcohol, is not ionized, but remains as a molecule, and on this the acid only slowly acts:

$$\underset{\text{(Alcohol)}}{R\cdot OH}+\underset{\text{(Acid)}}{(H^{\cdot}+Z')}=\underset{\text{(Ester)}}{R\cdot Z}+H_2O.$$

Not only are inorganic distinguished from ethereal salts in their ease of formation but also in their dissociability in solution, the former being usually entirely dissociated in solution, the latter not at all so. In this connection it is of great importance to point out that salts of organic acids with metals do undergo

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[1] This equation will serve as an example of how ions are represented in a reaction.

dissociation in solution and to about the same extent as inorganic salts. Thus in a solution of ethyl acetate there are no free ions, whereas in one of sodium acetate dissociation into $Na^{\cdot}$ and CH_3COO' ions occurs.

Mass Action. The formation of an ethereal salt when an alcohol and an acid are directly mixed, although slow, yet proceeds until a balance between the four constituents is established (i.e., between acid, alcohol, salt, and water). This is because the reaction is a reversible one; in other words, whenever a slight excess of ethereal salt comes to exist in the mixture, it decomposes by the action of water on it into the acid and alcohol, thus:

$$CH_3COOC_2H_5 + HOH \rightleftarrows CH_3COOH + C_2H_5OH.$$

Such *reversible reactions* are often represented in equations by two arrows in place of the sign of equality.

The amount of ester thus formed depends on the relative amounts of acid and alcohol present and not on the temperature. With a given amount of alcohol an increase in the amount of acid increases the yield of ethereal salt, and, conversely, the same is true with a given amount of acid when more alcohol is used. Since the progress of the formation of the above ester can be followed by titrating the residual acid, the reaction has been extensively employed in studying the laws of mass action.

The fundamental law of mass action states that the product of the number of gram-molecules per litre of the substances on the one side of the equation divided by the product of these on the other side is equal to some constant. In the case of the above reaction we have therefore the equation

$$\frac{C \text{ acid} \times C \text{ alcohol}}{C \text{ ester} \times C \text{ water}} = \text{constant},$$

where *C* represents gram-molecules per litre of the reacting substances.

It will be evident that if we increase *C* acid while *C* alcohol remains constant, then *C* ester must increase, which leads us to the conclusion that if enough acid be added all the alcohol will become converted into ester, or, conversely, that if more alcohol be added, the acid remaining constant, the same will be true.

Temperature does not affect the constant to any marked degree, i.e., does not influence the ultimate amount of ethereal salt produced. On the other hand, it greatly influences the rate of reaction, i.e., the time that it takes for the condition of chemical equilibrium to be reached. Thus a rise in temperature increases the velocity of the reaction (as a rule the rate doubles for each increase of ten degrees in temperature). By studying different alcohols and acids, it has been found that if equimolecular amounts of acid and alcohol be used the limit of esterification, i.e., the constant, varies only slightly, but the rate is much greater for such acids as acetic than it is for such as benzoic, and for primary than for secondary alcohols.

The amount of ester produced can be greatly increased by removing the water formed during the reaction, and in some cases this can be accomplished. By removing the ethereal salt as it is formed (e.g., by distillation or crystallization) much higher yields can also be obtained (see exp., p. 131).

Preparation of Ethereal Salts. The more usual methods for preparing ethereal salts are the following:

1. By heating a mixture of the acid and alcohol with sulphuric acid: ethylsulphuric acid is first formed and then reacts with the acid, sulphuric acid being re-formed (*cf.* ether, p. 91), thus:

$$(a)\quad C_2H_5\boxed{OH—H}\cdot HSO_4 = C_2H_5\cdot HSO_4 + H_2O.$$

$$(b)\quad C_2H_5\boxed{\cdot HSO_4—H}OOCCH_3 = C_2H_5—OOC\cdot CH_3 + H_2SO_4.$$

2. By heating a mixture of the acid and alcohol with hydrochloric acid gas: an acid chloride is probably first formed, which then reacts with the alcohol:

$$(a)\quad CH_3CO\boxed{OH + H}Cl = CH_3CO\cdot Cl + H_2O.$$

$$(b)\quad CH_3CO\boxed{Cl + H}OC_2H_5 = CH_3COO\cdot C_2H_5 + HCl.$$

3. Or the second stage of this reaction (*b*) can be itself used for the production of ethereal salts by treating an alcohol with an acid chloride or an anhydride of an acid. In this latter manner the acetyl or benzoyl (see p. 119) derivatives of many substances can be produced, and these, being readily purified, are extensively prepared for purposes of identification. The addition of sodium hydroxide accelerates this reaction in the case of benzoyl compounds (see p. 276).

4. By treating a silver salt of an acid with an alkyl halide (as iodide):

$$CH_3COO\boxed{Ag + I}C_2H_5 = CH_3COOC_2H_5 + AgI.$$

Properties. Esters in a pure state are stable; in watery solution they slowly decompose into acid and alcohol, the decomposition being greatly accelerated by boiling with water and by the action of acids or alkalies. Hydrolysis[1] most readily occurs with those esters which are easily formed; thus methyl acetate is more readily formed and is more easily hydrolyzed than ethyl acetate.

Many esters have pleasant odours, often simulating those of fruits. On this account some of them are used as artificial fruit essences (see p. 136).

Ethereal salts include the *neutral fats* (see p. 149). The two most important ethereal salts of acetic acid are methyl and ethyl acetates. Prepared by the general methods described above, both these bodies are liquids with pleasant odours. Ethyl acetate is commonly called acetic ether.

From a bio-chemical standpoint the acceleration which acids induce in the hydrolysis of esters is of interest, partly because a method for the quantitative determination of the acid in gastric juice is based on it, and partly because it typifies *catalytic action,* which is the means possibly by which ferments produce their actions.

If equimolecular quantities of different acids be added to similar quantities of methyl acetate, it will be found that the acceleration of hydrolysis produced varies greatly with the acid employed. HCl and HNO_3

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[1] Hydrolysis of esters is commonly called *saponification* (see p. 152).

produce about the greatest acceleration, whereas the commonest organic acids have only a feeble influence; thus the accelerating influence of oxalic acid is only 19% and of acetic only 0.4% of that of HCl. Now it has been found that the electrical conductivity of dilute solutions of the acids is directly proportional to their accelerating (catalytic) power, which leads us to the conclusion that the catalytic power depends on the amount of dissociation which the acids undergo; in other words, on the number of hydrogen ions existing in the solution (see p. 123). By this means, therefore, we have a practical method for gauging the relative strengths of acids (see p. 133).

Further, if we add dilute solutions of varying strengths of the same mineral acid to methyl acetate it will be found that the saponification is proportional to the strength of acid added. It is important to note that this law holds only for dilute solutions (less than decinormal) of strong acids and not at all for weak acids. By comparing the amount of saponification of methyl acetate which occurs when a known quantity of acid is added, with the amount occurring in a similar solution of methyl acetate having an unknown quantity of the same acid, an estimate can be made of the amount of acid actually present in the latter. In this comparison the two solutions must of course be kept at the same temperature and the action allowed to proceed for the same length of time (see exp. below).

EXPERIMENTS. (1) Put into a medium-sized flask 10 c.c. of alcohol and 10 c.c. of C.P. H_2SO_4. Use a two-hole cork; by one hole suspend a dropping funnel, by the other connect with a condenser. Place the flask in an oil-bath; record the temperature of the bath with a thermometer. Heat until the oil is at 140°, then begin running in slowly by the dropping funnel a mixture of 80 c.c. of alcohol and 80 c.c. of glacial acetic acid. Keep the temperature of the bath constant at about 140°. Regulate the inflow of acid alcohol to about correspond to the rate of distillation. Wash the distillate in the receiving flask with sodium carbonate solution until the top layer is no longer acid to litmus. Separate with a separating funnel. Add to the acetic ether a cold solution of 20 gm. of calcium chloride in 20 c.c. of water and shake. Separate with the funnel. Put the ethyl acetate into a dry flask, add solid calcium chloride, cork, and let it stand a day or so. Redistil on a water bath, noting the boiling-point (74.5° at 742 mm. barometric pressure). Determine the specific gravity (0.905 at 17°).

(2) Determine the rate of saponification of methyl acetate as influenced by different strengths of acid (HCl). Into each of two small flasks put 1 c.c. of methyl acetate measured accurately with a pipette; to one add with a pipette 20 c.c. of HCl solution of known strength (say 0.4%); to the other add 20 c.c. of HCl more dilute, but of unknown concentration; cork each flask and shake. As quickly as possible titrate 5 c.c. of each mixture successively with decinormal NaOH, using phenolphthalein as an indicator. This gives the acidity of each at the beginning of the experiment. Cork the flasks tightly and keep them in an incubator at about 40° for three or four hours, then, after shaking and cooling, take 5 c.c. from each and titrate again. The increase

in acid (due to acetic acid liberated by saponification) is found by deducting the initial titration from this second titration. The stronger solution causes the greater amount of saponification. To calculate the exact strength of the unknown acid solution by comparison with the known we must find out the limit of saponification for the known strength; to do this leave the flask containing this acid in the incubator for forty-eight hours, then titrate again. The titration at the end of this period, less the initial titration, gives an acid value called A; this is the number of cubic centimetres of decinormal acetic acid that can be liberated by saponification of the methyl acetate by 0.4% HCl. Now we can reckon the per cent of HCl in the other solution in the following manner: Find the value of the constant in the formula $C = \log\left(\frac{A}{A-X}\right)$ for each solution, but call the constant of the known solution C'. The observed increase in acid content during the three or four hours' incubation is X.

Take a particular experiment. A known solution (0.43435% HCl) gave $A = 24.9$ (c.c.). The increase (after four hours) in the known solution was 12.1 (c.c.), therefore $A - X = 24.9 - 12.1 = 12.8$:

$$C' = \log\left(\frac{24.9}{12.8}\right) = .2878.$$

With the unknown solution $X = 7$ (c.c.), $A - X = 17.9$:

$$C = \log\left(\frac{24.9}{17.9}\right) = .1430.$$

Now the per cent of HCl in the unknown

$$= \left(\frac{C \text{ of unknown}}{C' \text{ of known}}\right) \text{(per cent HCl in known).}$$

Therefore per cent $= \left(\frac{.1430}{.2878}\right)$ (0.43435) $=0.21544$.

In this particular case the unknown was of exactly half the strength of the known solution.

The rate of saponification bears a definite relation to the number of hydrogen ions present in the solution. Therefore with dilute solutions of easily ionizable acids (which are completely dissociated), as most mineral acids, an accurate estimation of the quantity of acid present can be made by this method. Most organic acids furnish so few hydrogen ions (see p. 109) that their presence has practically no effect. In consequence, the method is by all odds the best for determining the per cent of HCl present in gastric juice or stomach contents.

OTHER FATTY ACIDS.

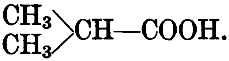
Propionic acid (propanoic acid), $CH_3 \cdot CH_2 \cdot COOH$, resembles acetic acid. It can be prepared in similar ways as the latter, namely, by oxidation of propyl alcohol, by hydrolysis of ethyl cyanide, and by the action of CO_2 on sodiumethyl. In addition it can be made by reduction of lactic acid, thus:

$$\underset{\textbf{(Lactic acid)}}{CH_3 \cdot CHOH \cdot COOH} + 2HI = CH_3 \cdot CH_2 \cdot COOH + H_2O + I_2.$$

The hydriodic acid furnishes nascent hydrogen, and this brings about reduction.

Corresponding to chloracetic acids there are chlorpropionic acids. But the halogen may take the place of hydrogen either in the CH_3 group or in the CH_2 group of propionic acid. It becomes necessary, therefore, to distinguish between these two positions in the molecule. This is done by using Greek letters, α and β. In order to have a rule which will apply to all acids, no matter how many carbon atoms the acid may contain, it is necessary to count backwards from the carboxyl group: thus, the group next to the COOH is in the α position, the second group is in the β position, and so on; for example, $CH_3 \cdot CHCl \cdot COOH$ is *α-chlorpropionic acid,* $CH_2Cl \cdot CH_2 \cdot COOH$ is *β-chlorpropionic acid.*

Butyric acid (butanoic acid), $CH_3 \cdot CH_2 \cdot CH_2 \cdot COOH$, is normal butyric acid.

Isobutyric acid or methylpropanoic acid has the formula  $\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!CH{-}COOH$. Normal butyric acid is fermentation butyric acid, and occurs in Limburger cheese, rancid butter, and sweat. It may be prepared by oxidation of butyl alcohol and by hydrolysis of propyl cyanide. Butter contains about five per cent of butyrin, which is the glycerol ester of butyric acid (see p. 146); the acid can therefore be obtained by hydrolysis or saponification of butter (see exp., p. 152). Microorganisms can cause fermentation of butter, with resulting hydrolysis of the ester (butyrin) and setting free of butyric acid. Butyric acid is soluble in water and volatile. Oleomargarine contains very little butyric or other soluble volatile fatty acids. On this account it can readily be identified by making an estimation of the volatile acids in the manner to be described later in an experiment (see p. 152).

Butyric acid can also be made from cane sugar as follows: The sugar solution, acidified with tartaric acid, is inoculated with sour milk: one variety of micro-organisms in the latter "inverts" the sugar into dextrose and lævulose; another variety ferments these monosaccharides, producing lactic acid; while a third variety converts the lactic acid into butyric acid:

$$\underset{\text{(Cane sugar)}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{(Dextrose)}}{C_6H_{12}O_6} + \underset{\text{(Lævulose)}}{C_6H_{12}O_6},$$

$$C_6H_{12}O_6 = \underset{\text{(Lactic acid)}}{2C_3H_6O_3},$$

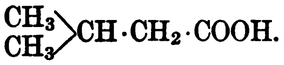
$$2C_3H_6O_3 = \underset{\text{(Butyric acid)}}{CH_3 \cdot CH_2 \cdot CH_2 \cdot COOH} + 2CO_2 + 2H_2.$$

Similar fermentation, with production of lactic and butyric acids, may occur in the stomach when the hydrochloric acid of the gastric juice is deficient in amount or absent altogether. The gases formed (CO_2 and H_2) cause the flatulence present in such cases. Butyric acid has the peculiar disagreeable odour characteristic of rancid butter.

The ethereal salt $C_3H_7 \cdot COOC_2H_5$, **ethyl butyrate,** resembles pineapple in odour. It is used as a flavouring material in place of pineapple juice.

Valeric acid (valerianic acid),

$$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot COOH,$$

is the normal acid. Ordinary valeric acid, however, is isovaleric acid,  $\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!CH \cdot CH_2 \cdot COOH$. It occurs in valerian root.

Amyl valerate, $C_4H_9 \cdot COOC_5H_{11}$, smells like apple, and is therefore used as an apple essence.

Caproic acid is $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot COOH$.

Of the higher fatty acids mention need be made only of **palmitic,** $C_{15}H_{31} \cdot COOH$, and **stearic,** $C_{17}H_{35} \cdot COOH$, both of which are contained in fats. They are insoluble and non-volatile. Palmitic acid melts at 60°, stearic acid at 68°.

CHAPTER XIII.

SECONDARY AND CERTAIN OTHER MONACID ALCOHOLS. KETONES

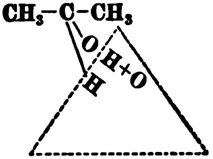
SECONDARY ALCOHOLS AND THEIR OXIDATION PRODUCTS.

Secondary alcohols contain the group CHOH, as in $CH_3 \cdot CHOH \cdot CH_3$, *secondary propyl alcohol.* None of the secondary alcohols is of any importance.

When a secondary alcohol is oxidized an aldehyde is not formed, but a *ketone:*

$$CH_3 \cdot CHOH \cdot CH_3 + O = CH_3 \cdot CO \cdot CH_3 + H_2O$$

or



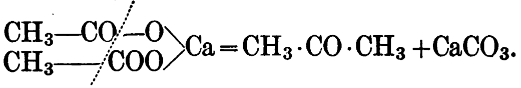
A **ketone** is in all essential points identical with an aldehyde, the only difference being that in the case of an aldehyde the oxygen atom is attached to a carbon atom at one end of the chain, while in a ketone it is attached to an inner carbon atom. Furthermore many ketones act as reducing agents toward alkaline silver and copper solutions. Some ketones give the fuchsin test (see p. 107). Many ketones form addition compounds with acid sulphites and with hydrocyanic acid (*cf.* aldehydes). Ketones do not polymerize, but they form condensation products.

The reaction of phosphorus pentachloride with ketones is similar to that with aldehydes:

$$CH_3\cdot CO\cdot CH_3 + PCl_5 = CH_3\cdot CCl_2\cdot CH_3 + POCl_3.$$

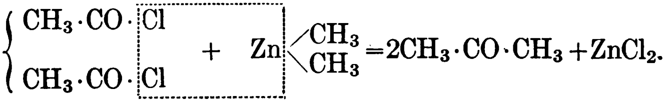
No hydrochloric acid is produced and a dichlor derivative is formed, therefore *a ketone does not contain hydroxyl.* The most important ketone is acetone.

Acetone (dimethylketone or propanone), $CH_3\,CO\cdot CH_3$, is the simplest ketone. It is produced by distilling calcium acetate,



$$\left.\begin{matrix}CH_3-CO-O\\ CH_3-COO\end{matrix}\right>Ca = CH_3\cdot CO\cdot CH_3 + CaCO_3.$$

It may also be obtained by oxidation of secondary propyl alcohol. Its synthesis from zinc methyl and acetyl chloride proves the structural formula for acetone:



$$\left\{\begin{matrix}CH_3\cdot CO\cdot Cl\\ \\ CH_3\cdot CO\cdot Cl\end{matrix}\right. + Zn\left<\begin{matrix}CH_3\\ CH_3\end{matrix}\right. = 2CH_3\cdot CO\cdot CH_3 + ZnCl_2.$$

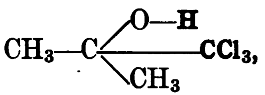
It is present in crude wood alcohol, and in the urine under certain conditions, especially in severe cases of diabetes. It is a useful solvent. Acetone is a liquid, boiling at 56.3° (corrected). Its specific gravity is 0.812 at 0°. Nascent hydrogen converts it into secondary propyl alcohol. It does not oxidize to an acid containing the same number of carbon atoms, but to acetic and formic or carbonic acids. Acetone gives the iodoform test.

Experiments. (1) Make iodoform, using acetone instead of alcohol (see p. 87).

(2) Dissolve 2 c.c. of acetone in very dilute H_2SO_4; add $KMnO_4$ solution until a pink colour remains on warming. Filter, make the filtrate strongly acid with 20% H_2SO_4, and distil. Test the distillate for acetic acid (see p. 115).

(3) Shake 5 c.c. of acetone with 5 c.c. of a strong solution of sodium bisulphite; cool; crystals of the addition compound of acetone appear.

Chloretone (chloroform acetone),



$CH_3-\overset{O-H}{\underset{CH_3}{C}}-CCl_3$,

is an addition product of acetone. It is formed by the interaction of acetone and chloroform in the presence of an excess of KOH. It is a useful hypnotic.

Sulphonal, another hypnotic, is produced from acetone (see p. 164).

Some acids are ketone acids containing both the carbonyl and carboxyl groups. **Aceto-acetic acid,** $CH_3 \cdot CO \cdot CH_2 \cdot COOH$, typifies these and is of importance, since it may occur in the urine (see p. 170).

Tertiary alcohols, when oxidized, decompose into compounds containing fewer carbon atoms than the alcohol. The tertiary alcohols are of no importance.

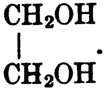
Little need be said of other monacid alcohols, except that most **waxes** are esters of monacid alcohols containing a large number of carbon atoms—for example, ceryl alcohol, $C_{27}H_{55}OH$, and melissic alcohol, $C_{30}H_{61}OH$.

CHAPTER XIV.

DIACID ALCOHOLS AND DIBASIC ACIDS.

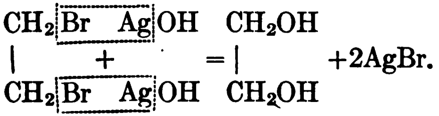
DIACID ALCOHOLS.

Diacid alcohols contain two hydroxyl groups. They are comparable to $Ca(OH)_2$. The simplest diacid alcohol and the only one of importance is **glycol** (ethandiol),



$$\begin{array}{l} CH_2OH \\ | \\ CH_2OH \end{array}$$

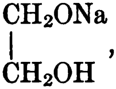
. The method of preparation shows that both hydroxyl groups are not attached to the same carbon atom. Ethylene is produced from ethyl alcohol by heating the latter with an excess of sulphuric acid. The ethylene is saturated with bromine, forming ethylene bromide, in the manner described in the experiment (see p. 230) From ethylene bromide glycol can be obtained by the action of silver hydroxide:



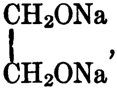
$$\begin{array}{lcl} CH_2\boxed{Br\ \ Ag}OH & & CH_2OH \\ | \qquad + & = & | \qquad\qquad +2AgBr. \\ CH_2\boxed{Br\ \ Ag}OH & & CH_2OH \end{array}$$

Glycol is a colourless glycerol-like liquid, of sweetish taste. It boils at 195° and has a specific gravity of 1.128 at 0°.

It forms two classes of ethereal salts, according to whether one or both hydroxyls are replaced. Similarly there are two sodium alcoholates of glycol:

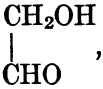


$$\begin{array}{l}CH_2ONa\\ |\\ CH_2OH\end{array}$$, monosodium glycolate.

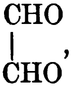


$$\begin{array}{l}CH_2ONa\\ |\\ CH_2ONa\end{array}$$, disodium glycolate.

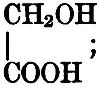
The oxidation products of glycol are numerous because of the presence of two primary alcohol groups. There are two aldehydes:

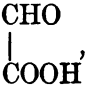
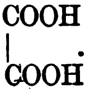


$$\begin{array}{l}CH_2OH\\ |\\ CHO\end{array}$$, glycolic aldehyde, and

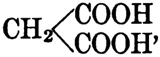
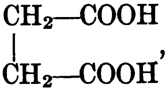
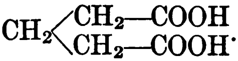


$$\begin{array}{l}CHO\\ |\\ CHO\end{array}$$, glyoxal.

Oxidation of the first gives rise to *glycolic acid,*  $\begin{array}{l}CH_2OH\\ |\\ COOH\end{array}$; this will be considered under hydroxy-acids (see p. 165).

Oxidation of glyoxal gives  $\begin{array}{l}CHO\\ |\\ COOH\end{array}$, *glyoxylic acid;* this is really a dihydroxy-acid, as will be seen later (see p. 171). These two acids are monobasic. Complete oxidation of glycol results in the formation of a dibasic acid, *oxalic acid,*  $\begin{array}{l}COOH\\ |\\ COOH\end{array}$.

DIBASIC ACIDS.

The simplest is *oxalic acid.* The next members of the series are *malonic acid,*  $CH_2\left<\begin{array}{l}COOH\\COOH\end{array}\right.$, *succinic acid,*  $\begin{array}{l}CH_2-COOH\\|\\CH_2-COOH\end{array}$, and *glutaric acid,*  $CH_2\left<\begin{array}{l}CH_2-COOH\\CH_2-COOH\end{array}\right.$.

General methods for the production of dibasic acids are (1) by hydrolysis of cyan-acids, (2) by oxidation of diacid alcohols, and (3) by oxidation of an hydroxy-acid.

Oxalic acid, $\begin{array}{l}COOH\\|\\COOH\end{array}$, forms crystals containing two molecules of water for each molecule of oxalic acid. The crystals readily effloresce. It may be prepared by oxidation of cane sugar with nitric acid. It is made commercially by heating sawdust with caustic potash and soda. Oxalic acid is one of the strongest of all organic acids, because its solution contains more hydrogen ions than the corresponding solutions of most other organic acids (see p. 123).

When oxalic acid is heated, it first loses its water of crystallization, then decomposes into carbon dioxide, carbon monoxide, water, and some formic acid. If heated in the presence of glycerol, formic acid and carbon dioxide are formed (see p. 112). Sulphuric acid decomposes it to carbon monoxide, carbon dioxide, and water. Potassium permanganate in warm acid solution oxidizes it to carbon dioxide:

$$2KMnO_4+5(COOH)_2+3H_2SO_4=10CO_2+K_2SO_4+2MnSO_4+8H_2O.$$

Oxalic acid forms two classes of salts, acid and neutral. *Acid potassium oxalate,* $\begin{array}{l}\mathrm{COOH}\\|\\\mathrm{COOK}\end{array}$, occurs in plants, particularly sorrel. *Ammonium, potassium,* and *sodium oxalates* are soluble; all other oxalates of metals are practically insoluble. *Calcium oxalate* frequently occurs in the urine as a crystalline sediment.

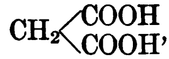
Oxalic acid is poisonous and has been used for suicidal purposes.

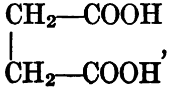
EXPERIMENTS. (1) *Preparation of oxalic acid.* Heat 200 c.c. of HNO_3 in a large flask to 100°. Set in a fume-closet and add 50 gm. of cane sugar. When the evolution of fumes has ceased, evaporate the acid mixture in an evaporating dish to about one fifth its original volume. Cool and collect the crystals. Recrystallize, using as little hot water as possible.

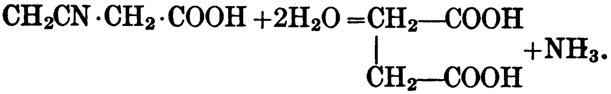
(2) Heat some dry crystals of oxalic acid in a test-tube—loss of water of crystallization occurs, as shown by drops collecting on the cool part of the tube.

(3) Decompose some oxalic acid with H_2SO_4; test the evolved gases for CO_2 (baryta water, as on p. 3) and CO (hæmoglobin solution, as on p. 113).

(4) To 5 c.c. of oxalic acid solution add a few drops of H_2SO_4, warm, then add potassium permanganate solution—it is decolorized.

Malonic acid,  $\mathrm{CH_2}\!<\!\begin{array}{l}\mathrm{COOH}\\\mathrm{COOH}\end{array}$, is of importance mainly in bringing about certain organic syntheses.

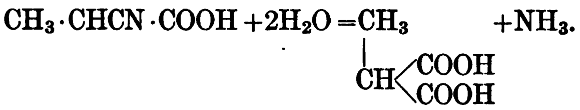
Succinic acid,  $\begin{array}{l}\mathrm{CH_2{-}COOH}\\|\\\mathrm{CH_2{-}COOH}\end{array}$, is *normal* succinic acid and may be produced by hydrolysis of β-cyanpropionic acid:



$$CH_2CN \cdot CH_2 \cdot COOH + 2H_2O = \begin{array}{l} CH_2—COOH \\ | \\ CH_2—COOH \end{array} + NH_3.$$

If caustic potash is used to effect hydrolysis, potassium succinate would be formed.

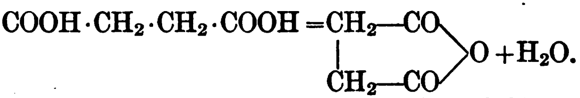
If α-cyanpropionic acid be hydrolyzed *iso*succinic acid is formed:



$$CH_3 \cdot CHCN \cdot COOH + 2H_2O = \begin{array}{l} CH_3 \\ | \\ CH \begin{array}{l} \diagup COOH \\ \diagdown COOH \end{array} \end{array} + NH_3.$$

These two acids give different reactions.

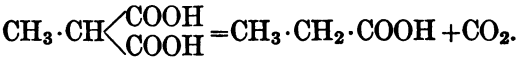
Normal succinic acid when heated to 235° yields *succinic anhydride* and water:



$$COOH \cdot CH_2 \cdot CH_2 \cdot COOH = \begin{array}{l} CH_2—CO \diagdown \\ | \qquad\qquad\; O \\ CH_2—CO \diagup \end{array} + H_2O.$$

(Succinic anhydride)

Isosuccinic acid, however, when heated above 130°, breaks up into propionic acid and carbon dioxide:



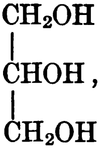
$$CH_3 \cdot CH \begin{array}{l} \diagup COOH \\ \diagdown COOH \end{array} = CH_3 \cdot CH_2 \cdot COOH + CO_2.$$

It is, indeed, a general rule in organic chemistry that two carboxyl groups cannot remain attached to the same carbon atom at high temperatures, carbon dioxide being split off from one of the carboxyls.

CHAPTER XV.

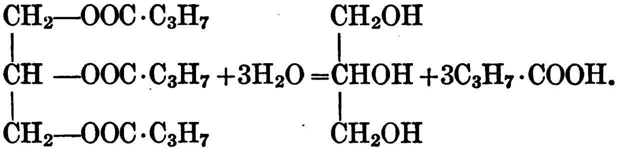
TRIACID ALCOHOLS, FATS, AND SOAPS.

TRIACID ALCOHOLS.



Glycerol (glycerine or propanetriol), $\begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array}$, is the only triacid alcohol of importance. Glycerol occurs in fats in combination with fatty acids and oleic acid, as glycerol esters of these acids. By hydrolyzing (i.e., saponifying) fats, glycerol is set free. This is accomplished commercially by heating fats in a closed boiler or autoclave with water and lime. The lime combines with fatty acids, forming insoluble calcium salts, while the glycerol goes into solution. The dilute glycerol solution is then distilled with superheated steam.

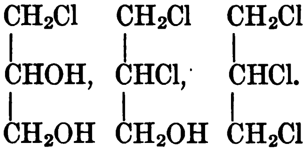
Glyceryl butyrate or butyrin yields on saponification glycerol and butyric acid, thus:



$$\begin{array}{l} CH_2—OOC\cdot C_3H_7 \\ | \\ CH\ —OOC\cdot C_3H_7 \\ | \\ CH_2—OOC\cdot C_3H_7 \end{array} + 3H_2O = \begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + 3C_3H_7\cdot COOH.$$

The other fats will be considered more fully presently.

Pure glycerol is a colourless, syrupy liquid, having a sweet taste. It boils at 290° and has a specific gravity of 1.265 at 15°. It is hygroscopic. Crystals of glycerol can be obtained by cooling to a low temperature (0°); these melt at 17°. It is volatile with water-vapour. It is useful as a solvent and as a preservative agent.

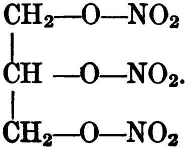
One, two, or three of the hydroxyl groups can be replaced by chlorine to form **mono-, di-, or trichlorhydrin** respectively:  $\begin{array}{l}CH_2Cl\\ |\\ CHOH,\\ |\\ CH_2OH\end{array}$ $\begin{array}{l}CH_2Cl\\ |\\ CHCl,\\ |\\ CH_2OH\end{array}$ $\begin{array}{l}CH_2Cl\\ |\\ CHCl.\\ |\\ CH_2Cl\end{array}$ If trichlorhydrin be heated with water to 170°, it is hydrolyzed to glycerol. Glycerol can be obtained from ethyl alcohol by producing successively acetic acid, acetone, isopropyl alcohol, propylene, propylene dichloride, trichlorhydrin, and finally glycerol:

$$\underset{\text{(Alcohol)}}{CH_3\cdot CH_2OH} \rightarrow \underset{\text{(Acetic acid)}}{CH_3\cdot COOH} \rightarrow \underset{\text{(Acetone)}}{CH_3\cdot CO\cdot CH_3} \rightarrow$$

$$\rightarrow \underset{\text{(Isopropyl alcohol)}}{CH_3\cdot CHOH\cdot CH_3} \rightarrow \underset{\text{(Propylene)}}{CH_3\cdot CH{=}CH_2} \rightarrow$$

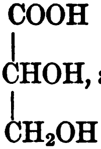
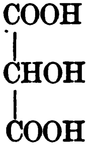
$$\rightarrow \underset{\text{(Propylene dichloride)}}{CH_3\cdot CHCl\cdot CH_2Cl} \rightarrow \underset{\text{(Trichlorhydrin)}}{CH_2Cl\cdot CHCl\cdot CH_2Cl} \rightarrow$$

$$\rightarrow \underset{\text{(Glycerol)}}{CH_2OH\cdot CHOH\cdot CH_2OH.}$$

Glycerol forms salts with nitric acid. The trinitrate is **nitroglycerine** or nitroglycerol. It is made by mixing glycerol with sulphuric and nitric acids. Its formula is  $\begin{array}{l}CH_2—O—NO_2\\ |\\ CH\ —O—NO_2.\\ |\\ CH_2—O—NO_2\end{array}$ It explodes when suddenly heated or percussed, with the formation of nitrogen, nitric oxide, carbon dioxide, and water. It is a yellow, oily liquid. **Dynamite** consists of infusorial earth or other material impregnated with nitroglycerol, and may contain as much as 75% of the latter.

Nitroglycerol is a strong poison, causing violent headache and lowering of blood-pressure. In appropriate dosage it is extremely useful as a medicine.

Glycerol forms glyceryl acetates when treated with acetic anhydride. This will be considered more fully under fats.

On oxidation glycerol yields *glyceric acid*,  $\begin{array}{l}\mathrm{COOH}\\ |\\ \mathrm{CHOH},\\ |\\ \mathrm{CH_2OH}\end{array}$ and *tartronic acid*,  $\begin{array}{l}\mathrm{COOH}\\ |\\ \mathrm{CHOH}.\\ |\\ \mathrm{COOH}\end{array}$ These are studied with the hydroxy-acids (see pp. 171 and 173).

EXPERIMENTS. (1) Heat 1 c.c. of glycerol with 5 gm. of $KHSO_4$ in an evaporating dish until it turns brown. Note the odour (acrolein).

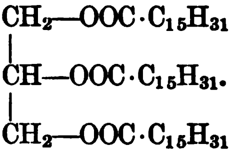
(2) Repeat the same experiment, using lard or some other fat.

(3) To a few cubic centimetres of NaOH solution add $CuSO_4$ until a copious precipitate of $Cu(OH)_2$ is obtained; now add some glycerol and shake—a deep-blue solution results.

FATS AND SOAPS.

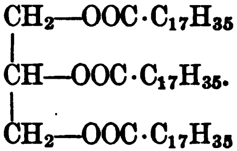
Fats are ethereal salts of glycerol with fatty acids and with the unsaturated acid, oleic acid. Most fats are mixtures of *palmitin* (glyceryl tripalmitate), *stearin* (glyceryl tristearate), and *olein* (glyceryl trioleate). Olein is a liquid. Stearin has the highest melting-point (about 66°). Mutton-fat contains a large percentage of stearin. The softer fats contain less stearin and relatively more palmitin and olein. Physiologically, the fats of lower melting-point are more easily digested.

Palmitin is



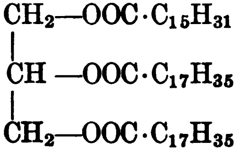
$$\begin{array}{l} CH_2-OOC\cdot C_{15}H_{31} \\ | \\ CH-OOC\cdot C_{15}H_{31}. \\ | \\ CH_2-OOC\cdot C_{15}H_{31} \end{array}$$

Stearin is



$$\begin{array}{l} CH_2-OOC\cdot C_{17}H_{35} \\ | \\ CH-OOC\cdot C_{17}H_{35}. \\ | \\ CH_2-OOC\cdot C_{17}H_{35} \end{array}$$

Mixed esters of glycerol can be obtained; some have been proven to occur naturally.



$$\begin{array}{l} CH_2-OOC\cdot C_{15}H_{31} \\ | \\ CH-OOC\cdot C_{17}H_{35} \\ | \\ CH_2-OOC\cdot C_{17}H_{35} \end{array}$$

is a mixed ester.

Some vegetable fats and oils contain glycerol esters of other acids than stearic, palmitic, and oleic acids.

These three acids are insoluble and non-volatile. Butter contains glycerol esters of fatty acids which are *volatile* and *soluble*, namely, butyric, capric, caprylic, and caproic acids. Artificial butters (as oleomargarine) contain only very small amounts of these acids.

Fat Values. By determining certain analytical values[1] and by finding the melting-point and specific gravity, a fat can generally be identified with the aid of the tables compiled for the purpose. The values referred to will now be briefly explained in order.

(1) The *Reichert-Meissl value* indicates the amount of volatile soluble acid present in the fat. When butter or any other fatty substance is saponified so as to free the fat acid and then distilled as described in the experiment below, the volatile acid in the distillate can be readily estimated by titration. The Reichert-Meissl value is the number of cubic centimetres of decinormal acid contained in the distillate from five grams of fatty substance.

(2) The *acid value* of a fat is found by titration of a solution of the fat in alcohol with decinormal KOH, using phenolphthalein as an indicator. This determines the amount of free acid present. The acid value is expressed as milligrams of KOH required to neutralize the free acids in one gram of fat.

(3) The total amount of acid present, free and combined, is indicated by the *saponification value.* A weighed quantity of fat is saponified with the aid of an accurately measured quantity of KOH solution of

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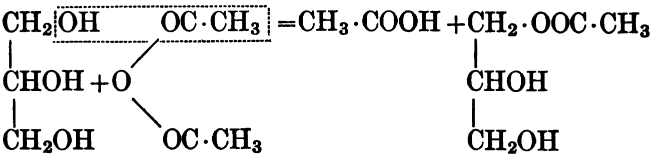
[1] A very satisfactory book on this subject is Chemical Analysis of Oils, Fats, and Waxes, by *J. Lewkowitsch* (new edition, 1905).

known strength; the resulting soap is diluted and titrated to find how much KOH remains unneutralized. Then the amount in milligrams of KOH combined with fatty acid as soap for each gram of fat taken is readily calculated; this is the saponification value.

(4) The *ether value* of a fat represents the combined acid, being the saponification value less the acid value.

(5) The *iodine value* estimates the amount of unsaturated acid (e.g., oleic) present.

(6) The *acetyl value* estimates the hydroxyl content. If glycerol be treated with acetic anhydride, one molecule of acetic acid is produced for each hydroxyl group attached (see p. 121):



(Glyceryl monacetate)

The reaction can be pushed until all of the hydroxyl groups are displaced, giving, as the products, glyceryl triacetate and acetic acid (three molecules of the latter for each molecule of glycerol). In a similar manner a fat which contains some hydroxyl groups can be "acetylated," and by estimating the acetic acid in combination with the alcohol, or acids of the fat, the hydroxyl content can be calculated. This would not be applicable to common fats, but mainly to fats containing hydroxy-acids.

EXPERIMENTS. (1) Compare the specific gravity of filtered butter and oleomargarine by successively putting a little of each in alcohol of specific gravity 0.926 at 15°. The oleomargarine will float (it having a specific gravity of about 0.918 at 15°); the butter will either sink or remain suspended.

(2) *Reichert-Meissl value.* Into a small flask put 5 gm. of filtered butter, 2 c.c. of 70% KOH solution, and 10 c.c. of alcohol (free of acid or aldehyde). Attach to a reflux condenser and heat on a water bath for fifteen minutes. Distil off the alcohol. Add 100 c.c. of distilled water and heat until the soap is dissolved. Add 40 c.c. of 5% H_2SO_4 and some small pieces of pumice.[1] Distil on a sand bath. Collect 110 c.c. of distillate in a graduated flask. Filter the distillate; take 100 c.c. of the filtrate with a pipette and transfer it to a beaker. Add a little phenolphthalein solution and titrate with decinormal NaOH until slightly pink. Multiply the number of cubic centimetres of alkali by 1.1; this gives the Reichert-Meissl value. For butter this value should not be less than 24. The experiment may be repeated with oleomargarine.

When fats are hydrolyzed with the aid of alkali, **soap** is formed. Hence the origin of the term *saponification.* In the strict sense, saponification means hydrolysis of an ethereal salt, the resulting products being an alcohol and an acid. Many use the word loosely instead of hydrolysis.

Soaps are salts of the fatty acids which occur in fats with metals. Ordinary soaps are mixtures of potassium or sodium palmitate, stearate, and oleate. Potassium soap is soft soap, commonly dispensed as green soap. It is of a yellow colour, but in many countries this colour is changed to green by the addition of indigo. It contains the glycerol that is freed by saponification. Sodium soap is hard soap. It is freed of glycerol by "salting out" in the manner described in the experiment. Castile or Venetian soap, if genuine, is made from olive oil. It is slightly yellow in colour. Calcium, mercury, lead, copper, and many other metals form insoluble soaps.

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[1] To prevent bumping.

The *cleansing action* of soap is due to the presence of free alkali in dilute soap solution. Hydrolytic dissociation of soap can be demonstrated as follows: Add phenolphthalein to a concentrated soap solution, and only a slight red colour appears; now dilute with a large quantity of water, when a decided red colour develops (for effect of dilution on dissociation, see p. 53). Dirt is held on the skin or clothing by the aid of fatty material; the alkali partly saponifies and partly emulsifies this, with the result that the "grease" can now be rinsed off. The lather also aids mechanically in removing dirt.

EXPERIMENTS. (1) Melt in an evaporating dish about 10 gm. of lard or tallow, add 100 c.c. of 20% KOH and 50 c.c. of alcohol, and boil moderately. After boiling half an hour test by shaking a drop of the fluid with half a test-tube of water; if no oily drops separate out, saponification is complete. Boil until completely saponified, adding water as necessary to maintain constant volume. Pour into a large beaker; when partly cooled add a saturated solution of NaCl. Sodium soap will separate as a top layer and finally solidify.

(2) To same soap solution add hydrochloric acid. Free fatty acids separate and rise to the top. Collect the fatty acids on a filter, wash thoroughly with water, press between filter paper, and crystallize from hot alcohol.

(3) Make insoluble soap by treating same soap solution with calcium chloride solution (calcium soap), with lead acetate (lead soap), copper sulphate, and solutions of other metallic salts.

CHAPTER XVI.

NITROGEN DERIVATIVES. (ALSO PHOSPHORUS AND SULPHUR COMPOUNDS.)

NITROGEN DERIVATIVES.

THESE fall into three classes: (1) cyanogen derivatives, (2) substituted ammonias, and (3) nitro compounds.

Cyanogen Derivatives. Organic cyanides can be prepared by treatment of alkyl halides with potassium cyanide, as

$$\underset{\text{(Ethyl chloride)}}{C_2H_5\boxed{Cl+K}}CN = \underset{\text{(Ethyl cyanide)}}{C_2H_5CN} + KCl,$$

also by anhydrolysis (removal of water) of an acid amide (see p. 186), thus (see exp.):

$$\underset{\text{(Acetamide)}}{CH_3\cdot CONH_2} = \underset{\text{(Methyl cyanide)}}{CH_3\cdot CN} + H_2O.$$

EXPERIMENT. Into a small dry fractionating flask put 5 gm. of dry acetamide and add quickly about 7.5 gm. of phosphorus pentoxide. Cork and connect with a condenser immediately. Heat with a small smoky flame. Collect the distillate in a large clean test-tube. Shake the distillate with half its volume of water, then add small pieces of solid KOH until no more dissolves, keeping the solution cool with running water. Remove the top layer of cyanide carefully with a clean dry pipette. Run it into a small fractionating flask; add some P_2O_5 and redistil. Note the boiling-point (82°).

The CN group of organic cyanides can be hydrolyzed to COOH; in conscquence they are called acid *nitriles;* for example, $CH_3 \cdot CN$ is acetonitrile because acetic acid can be obtained from it (see exp., p. 122):

$$CH_3CN + 2H_2O = CH_3 \cdot COOH + NH_3.$$

HCN, *hydrocyanic acid,* may be called formonitrile because it can be hydrolyzed to formic acid. It is very poisonous, but is used in dilute solution as a remedy.

This reaction also shows that the carbon atom of CN is linked directly to the carbon chain. There are cyanides, however, in which it is the nitrogen atom of the CN group that is linked to the carbon chain. These are **isocyanides.** $CH_3—N \equiv C$ is *methyl isocyanide.* Curiously enough, silver alone of all the metals forms with CN not a cyanide, but an isocyanide:

$$AgNO_3 + K—C \equiv N = Ag—N \equiv C + KNO_3.$$

Isocyanides may therefore be produced by the aid of silver cyanide:

$$Ag—N \equiv C + \underset{\text{(Methyl iodide)}}{CH_3 \cdot I} = AgI + \underset{\text{(Methyl isocyanide)}}{CH_3 \cdot N \equiv C}.$$

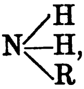
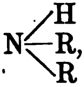
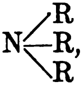
Chloroform when heated with alkali and an amide gives rise to the disagreeable vapour of isocyanide:

$$CHCl_3 + R—NH_2 = R—NC + 3HCl.$$

When an isocyanide is hydrolyzed, an amide and formic acid are formed:

$$CH_3 \cdot NC + 2H_2O = CH_3NH_2 + HCOOH.$$

EXPERIMENT. *Isocyanide reaction.* Mix together in a test-tube a few drops of chloroform, 1 c.c. of aniline, and 2 c.c. of alcoholic KOH. Warm gently. Note the peculiar disagreeable odour of the isocyanide. As soon as detected dilute the mixture with much water in the sink, since the fumes are poisonous.

Substituted Ammonias. These may be considered as ammonia in which one or more hydrogen atoms are replaced by organic groups. *Primary substituted ammonias,*  contain the group NH_2, called the amido or amino group. *Secondary substituted ammonias,*  contain the imido group, NH. *Tertiary substituted ammonias,*  have all the hydrogen of ammonia displaced.

These are all called **amines.** They are prepared by the action of ammonia on alkyl halides:

$$C_2H_5Br + NH_3 = \underset{\text{(Ethylamine)}}{C_2H_5NH_2 \cdot HBr},$$

$$C_2H_5NH_2 + C_2H_5Br = \underset{\text{(Diethylamine)}}{(C_2H_5)_2NH \cdot HBr},$$

$$(C_2H_5)_2NH + C_2H_5Br = \underset{\text{(Triethylamine)}}{(C_2H_5)_3N \cdot HBr}.$$

The HBr is removed by treating the above compounds with KOH.

The amines may also be prepared by treating an acid amide with sodium hypobromite (see exp.):

$$\underset{\text{(Acetamide)}}{CH_3\cdot CONH_2} + Br_2 + 4NaOH = \underset{\text{(Methylamine)}}{CH_3\cdot NH_2} + 2NaBr + Na_2CO_3 + 2H_2O.$$

(Br forms hypobromite with NaOH.)

Experiment. Treat 12.5 gm. of dry acetamide in a half-litre flask with 11.5 c.c. of bromine; add a cooled solution of 20 gm. of KOH in 175 c.c. of water until the mixture turns a bright yellow, meanwhile keeping the flask cooled with running water. Run this hypobromite mixture by means of a dropping funnel rapidly into a solution of 40 gm. of KOH in 75 c.c. of water. Keep the temperature of the liquid at 70°–75°. Cool the flask if the temperature gets above 75°. Keep at 75° for thirty minutes. Add some powdered pumice and distil on a sand bath. Attach an adapter (see fig. 19, p. 83) to the condenser; dip this slightly below the surface of strong hydrochloric acid in the receiving flask (50 c.c. C.P. HCl + 50 c.c. of water). Distil until the distillate, tested by detaching the adapter momentarily, is no longer strongly alkaline to litmus. Evaporate the acidulated distillate in an evaporating dish heated over wire gauze. When down to small bulk complete the drying in an oven at 110°. Pulverize the residue; treat with several portions of 10 c.c. of hot alcohol, filtering the decanted alcohol into a dry beaker. Crystals of methylamine hydrochloride separate out by cooling.

Filter off the crystals; press between filter-paper; keep part as a specimen. Put the rest into a small test-tube, add strong KOH solution; methylamine is evolved. Note the odour and the reaction of the gas to litmus Test its inflammability by corking the test-tube with a cork fitted with a glass tube which has a finely drawn tip, and applying a flame to this tip. Heat the mixture if necessary to secure free evolution of gas.

Nascent hydrogen converts an alkyl cyanide into an amine,

$$\underset{\text{(Methyl cyanide)}}{CH_3CN} + 4H = \underset{\text{(Ethylamine)}}{CH_3 \cdot CH_2NH_2}.$$

Many amines, particularly the primary ammonia bases, are decomposed by nitrous acid. This is a reaction of considerable importance. An ammonium nitrite derivative is formed first, but this is so unstable that it breaks down, liberating nitrogen:

$$\underset{\text{(Ethylamine)}}{NH_2 \cdot C_2H_5} + HNO_2 = \underset{\text{(Ethyl ammonium nitrite)}}{NH_3(C_2H_5) \cdot NO_2},$$

$$NH_3(C_2H_5) \cdot NO_2 = N_2 + H_2O + C_2H_5OH.$$

Many amines result from decomposition of proteid material. Amines resemble ammonia in odour, and their vapours are alkaline to litmus. When dissolved in water they form bases, i.e., they give rise to hydroxyl ions. Many of the amines are more strongly basic than ammonium hydroxide.

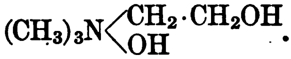
There are **quaternary bases** in which four organic groups are linked to nitrogen; these are really substituted ammonium compounds. *Tetramethyl ammonium hydroxide* is $(CH_3)_4NOH$ (cf. NH_4OH). This is a very strong base; its saponifying power is almost equal to that of sodium hydroxide. If the saponifying power of LiOH be taken as 100,

$$\begin{aligned} \text{KOH and NaOH} &= 98 \\ (CH_3)_4NOH &= 75 \\ NH_4OH &= 2 \end{aligned}$$

Methylamine, dimethylamine, and **trimethylamine** are gases. They are contained in herring-brine. They are also obtained by destructive distillation of the residue which is left after preparing alcohol from the molasses of beet sugar. HCl is used to hold the amines as salts. This amine distillate is used commercially to produce methyl chloride, because the latter can be obtained from trimethylamine by treatment with hydrochloric acid:

$$(CH_3)_3N—HCl + 3HCl = 3CH_3Cl + NH_4Cl.$$

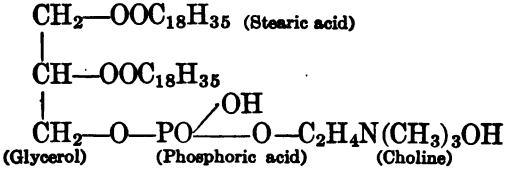
Choline is a substituted ammonium hydroxide, related to trimethylamine:



$$(CH_3)_3N\begin{matrix} \diagup CH_2\cdot CH_2OH \\ \diagdown OH \end{matrix}.$$

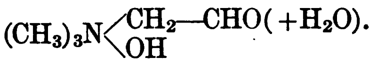
It will be noticed that it is also related to primary alcohols. It is of physiological importance.

The **lecithins** are salts of choline. The principal lecithin contains stearic and glycerophosphoric acids in combination with choline, having the formula



Lecithin is an important constituent of nerve-tissue, of bile, and of the envelope of red blood-corpuscles.

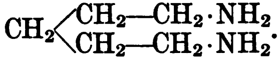
Muscarine is closely related to choline. It has been suggested that it is the aldehyde corresponding to choline considered as an alcohol:



$$(CH_3)_3N\begin{matrix}\diagup CH_2\text{—}CHO(+H_2O).\\ \diagdown OH\end{matrix}$$

It is a basic substance classed as an alkaloid (see p. 328). Muscarine is very poisonous and is contained in toadstools (*Agaricus muscarius*) and some other plants.

Many **ptomaines**[1] are amine bases. Methylamine, dimethylamine, trimethylamine, ethylamine, diethylamine, triethylamine, propylamine, butylamine, amylamine, muscarine, and choline occur as ptomaines. **Cadaverine** is a diamine ptomaine,

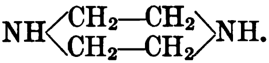


$$CH_2\begin{matrix}\diagup CH_2\text{—}CH_2\cdot NH_2\\ \diagdown CH_2\text{—}CH_2\cdot NH_2\end{matrix}.$$

Neurine, like choline, is a ptomaine containing oxygen,

$$(CH_3)_3\cdot NC_2H_3\cdot OH.$$

Urotropine is hexamethylentetramine, $(CH_2)_6N_4$, and is obtained by the action of ammonia on formaldehyde.

Piperazine is diethylendiamine,  $NH\begin{matrix}\diagup CH_2\text{—}CH_2\diagdown\\ \diagdown CH_2\text{—}CH_2\diagup\end{matrix}NH.$ Urotropine and piperazine act as solvents for uric acid

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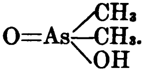
[1] Ptomaines are organic bases formed by the action of bacteria on nitrogenous matter. Decomposing animal tissue is very apt to contain ptomaines. Many of them are highly toxic and are the cause of death in certain cases of poisoning by canned meats, etc.

(in a test-tube at least). *Sidonal*, *lycetol*, and *lysidin* are piperazine derivatives and are used for the same purpose.

Analogous to the substituted ammonias are the substitution derivatives of phosphine (PH_3) and arsine (AsH_3). Since they will be mentioned in no other place, it may be well in this connection to state that there are organic acids containing phosphorus or arsenic, as, for example, *cacodylic acid*, which is dimethylarsenic acid,



Furthermore, there are a number of phosphorus-containing substances which are of importance in physiological chemistry, such as lecithin (see p. 160) and its constituent glycerophosphoric acid, phosphatides (substances obtained from brain-tissue which contain the phosphoric acid radicle but no glycerophosphoric acid), nucleins and pseudonucleins, paranucleic and other nucleic acids, phosphocarnic acid, nucleoalbumins, phosphoglobulins, phosphoglucoproteids, etc.

Nitro Compounds.—The nitro compounds of the benzenes are much more important than are those of the paraffins, and will be considered later.

Of the paraffins the only important nitro compounds are **ethyl nitrite,** $C_2H_5—O—NO$, and **amyl nitrite,** $C_5H_{11}—O—NO$. Both are used as medicines. Amyl nitrite is a very valuable remedy; its physiological action is similar to that of nitroglycerol (see p. 147), but comes on quickly and is very evanescent. It can be prepared as described in the experiment below.

EXPERIMENT. Prepare amyl nitrite as follows: Mix in a small flask 20 c.c. of amyl alcohol and 15 gm.

of finely powdered sodium nitrite. Set the flask in ice-water; add to the alcohol, drop by drop, 5 c.c. of C.P. H_2SO_4 from a dropping funnel. Amyl nitrite forms a top layer; decant it off into a separating funnel. Add some water to the mixture in the flask and shake; more amyl nitrite separates out; decant again. Separate the nitrite from the aqueous liquid. Dry with calcium chloride and distil. Note the colour, odour, and the effect of cautious inhalation (flushing of the face and vascular throbbing).

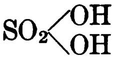
SULPHUR DERIVATIVES.

Sulphur may take the place of oxygen in alcohols or ethers, forming **sulphur alcohols** and **ethers,** as

$$CH_3 \cdot SH \ (cf.\ CH_3OH),$$
$$CH_3 \cdot S \cdot CH_3 \ (cf.\ CH_3OCH_3).$$

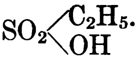
Sulphur alcohols are called mercaptans. When they are oxidized, as with nitric acid, **sulphonic acids** are formed, $CH_3 \cdot SH + 3O = CH_3 \cdot SO_3H$. The sulphonic acid group is SO_3H.

Sulphonic acids may be looked upon as sulphuric acid in which an hydroxyl group is replaced by an organic group:



$$SO_2\left<\begin{matrix}OH\\OH\end{matrix}\right.$$

(Sulphuric acid)

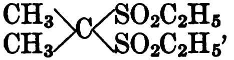


$$SO_2\left<\begin{matrix}C_2H_5.\\OH\end{matrix}\right.$$

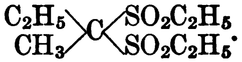
(Ethylsulphonic acid)

The sulphonic acids are of more importance in the chemistry of aromatic compounds.

There are three aliphatic sulphonic derivatives of importance, because they are used as hypnotics.

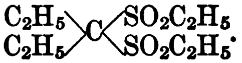
Sulphonal (sulphonmethane), diethylsulphonedimethylmethane,  $\begin{matrix}CH_3\\CH_3\end{matrix}>C<\begin{matrix}SO_2C_2H_5\\SO_2C_2H_5\end{matrix}$, is made from acetone and ethyl mercaptan. It forms colourless crystals, slightly soluble in cold water, quite soluble in hot water.

Trional (sulphonethylmethane) is



$$\begin{matrix}C_2H_5\\CH_3\end{matrix}>C<\begin{matrix}SO_2C_2H_5\\SO_2C_2H_5\end{matrix}.$$

Tetronal is



$$\begin{matrix}C_2H_5\\C_2H_5\end{matrix}>C<\begin{matrix}SO_2C_2H_5\\SO_2C_2H_5\end{matrix}.$$

CHAPTER XVII.

MIXED COMPOUNDS. HYDROXY-ACIDS.

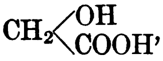
Under mixed compounds we shall consider hydroxy-acids, amido compounds, and carbohydrates.

Hydroxy-acids contain both alcohol (OH) and acid (COOH) groups. The acid properties, however, are more marked than the alcohol properties. They are not acid alcohols, but hydroxy-acids, and may therefore be defined as acids in which a hydrogen atom attached to one of the carbon atoms is replaced by hydroxyl. They are often called oxy-acids.

The simplest possible hydroxy-acid would be *hydroxy-formic acid,*

$$\underset{\text{(Formic acid)}}{H\cdot COOH} \rightarrow \underset{\text{(Hydroxy-formic acid)}}{HO\cdot COOH}.$$

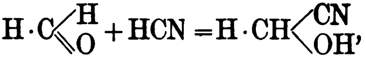
It will be observed that this is identical with the hypothetical carbonic acid, H_2CO_3.

The lowest typical hydroxy-acid is hydroxyacetic acid,  $CH_2\langle{}^{OH}_{COOH}$, or glycolic acid (mentioned previously under glycol).

Glycolic acid (ethanolic acid) may be prepared in many ways, starting either with an alcohol or an acid:

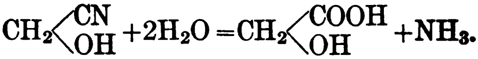
(1) By oxidation of glycol or glycol aldehyde (see p. 142).

(2) By forming the cyanogen derivatives of methyl alcohol, or, what is the same thing, the cyanhydrin of formaldehyde, then hydrolyzing:



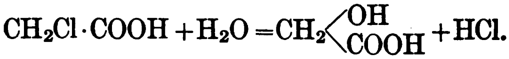
$$H\cdot C\left\langle\begin{matrix}H\\O\end{matrix}\right. + HCN = H\cdot CH\left\langle\begin{matrix}CN\\OH\end{matrix}\right.,$$

(Cyanhydrin of formaldehyde)



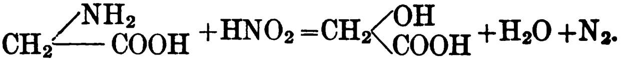
$$CH_2\left\langle\begin{matrix}CN\\OH\end{matrix}\right. + 2H_2O = CH_2\left\langle\begin{matrix}COOH\\OH\end{matrix}\right. + NH_3.$$

(3) By boiling monochloracetic acid with water:



$$CH_2Cl\cdot COOH + H_2O = CH_2\left\langle\begin{matrix}OH\\COOH\end{matrix}\right. + HCl.$$

(4) By treating aminoacetic acid (glycocoll) with nitrous acid:



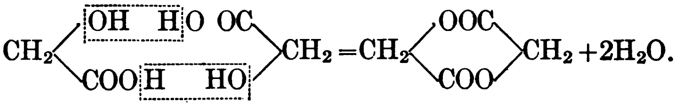
$$CH_2\left\langle\begin{matrix}NH_2\\COOH\end{matrix}\right. + HNO_2 = CH_2\left\langle\begin{matrix}OH\\COOH\end{matrix}\right. + H_2O + N_2.$$

(Glycocoll)

These methods are in general applicable to other hydroxy-acids.

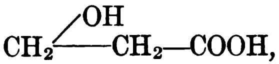
Glycolic acid (as also other hydroxy-acids) forms ethereal salts similar not only to salts of other acids, but also to salts of alcohols. There is ethyl glycolate, $CH_2\left\langle\begin{matrix}OH\\COO\cdot C_2H_5\end{matrix}\right.$, and ethyl-glycolic acid, $CH_2\left\langle\begin{matrix}OC_2H_5\\COOH\end{matrix}\right.$, also glycolic acetate, $CH_2\left\langle\begin{matrix}OOC\cdot CH_3\\COOH\end{matrix}\right.$.

Glycolic acid is found in green grapes and elsewhere. It forms needle crystals, melting at 80°. It is a stronger acid than acetic acid. When heated in an atmosphere of carbon dioxide at 210° it combines with itself, losing water, thus forming an anhydride called *glycolid:*



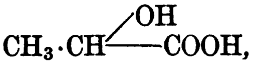
This has neither alcoholic nor acidic properties.

Hydroxypropionic acids are commonly called **lactic acids.** Just as there are two monochlorpropionic acids, α and β, so there is an α-hydroxypropionic acid and a β-hydroxypropionic acid. The β acid,

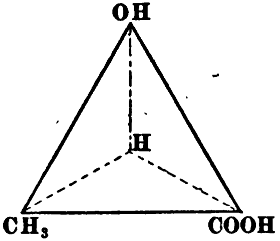


shows by its reactions that it is related to ethylene (see p. 230). It is therefore called ethylene lactic acid. It is unimportant.

Lactic acid proper, *α-hydroxypropionic acid,*



is known in three forms as isomers. As with amyl alcohol, these isomers have identical structural formulæ. Isomerism of the kind to be described now is called *physical* or *stereoisomerism.* To understand this it is necessary to conceive of the atoms of the molecules as being arranged in space, and not on one plane as in ordinary formulæ. The main carbon atom is thought of as being placed in the centre of a tetrahedron, at the apex of each solid angle of which is situated an atom or group. Models of wood or pasteboard will be helpful in understanding this. To represent α-lactic acid, write the groups CH_3, OH, H, and COOH at the corners of the tetrahedron, thus:



Try the effect of interchanging these groups in all possible ways. It will be found that two and only two different arrangements are possible.[1] Further, by holding the tetrahedron representing one combination before a mirror, the image in the mirror will be seen to correspond exactly to the other possible arrangement. This is true only in the case of compounds which would be represented as having four *different* groups at the corners. If two of these groups are the same, only one arrangement is possible and stereoisomerism cannot occur.

The tetrahedron representing lactic acid is unsymmetrical as regards the kind of groups present; its central carbon atom is therefore said to be an *asymmetric* carbon atom. It has been found that compounds containing an asymmetric carbon atom rotate the plane of polarized light. Dextrolactic acid rotates it to the right, lævolactic acid rotates it to the left. As represented by models lævolactic acid is the mirror-image of dextrolactic acid. Ordinary lactic is also an α-lactic acid, but it does not affect polarized light; it is optically inactive. It has been shown to consist of a mixture of an equal number of dextrolactic and lævolactic acid molecules; such a substance is called *racemic.* The two constituent acids of racemic acid neutralize each other in their action on polarized light.

---

[1] The truth of this statement can be most clearly shown by writing down the various possible arrangements and then marking off those that are identical.

Dextrolactic acid (*d*-lactic acid) is also called *sarcolactic acid,* because it occurs in flesh. It is present in beef extract. It is also the product of fermentation of dextrose by the *Micrococcus acidi paralactici.* Its salts are lævorotatory.

Lævolactic acid (*l*-lactic acid) is obtainable by fermentation of dextrose by the *Micrococcus acidi lævolactici.*

Racemic lactic acid (*i*-lactic acid) is a syrupy liquid having a specific gravity of 1.2485 at $\frac{15^\circ}{4^\circ}$. It is stronger than most organic acids. It is the product of ordinary lactic acid fermentation. When milk sours, milk-sugar becomes converted into lactic acid by microörganisms:

$$\underset{\text{(Lactose)}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{(Lactic acid)}}{4C_3H_6O_3}.$$

No matter in what way lactic acid is artificially produced by synthesis, the synthetic acid is always racemic. An optically active substance has never yet been synthesized by purely chemical methods from inactive substances; in other words, the influence of living cells seems to be essential for the obtaining at first hand of optically active substances. *i*-Lactic acid can be shown to contain dextrolactic acid by growing the mould *Penicillium glaucum* in a solution of *i*-ammonium lactate: the mould destroys the lævolactic acid. It may be shown to contain lævolactic acid by fractional crystallization of a solution of strychnine lactate, inasmuch as the lævolactate crystals are formed first.

When heated to 150° in dry air lactic acid changes to an anhydride called lactid (*cf.* glycolic acid, p. 167). Hydriodic acid reduces lactic acid to propionic acid, (see p. 134).

EXPERIMENT. In a retort mix 5 c.c. of lactic acid, 10 c.c. of water, and 5 c.c. of concentrated H_2SO_4. Connect with a condenser. Heat with a smoky flame. Test the distillate for aldehyde (see p. 106) and for formic acid (see p. 113):

$$CH_3\cdot CHOH\cdot COOH = CH_3\cdot CHO + H\cdot COOH.$$

β-Hydroxybutyric acid (β-oxybutyric acid),

$$CH_3\cdot CH(OH)\cdot CH_2\cdot COOH,$$

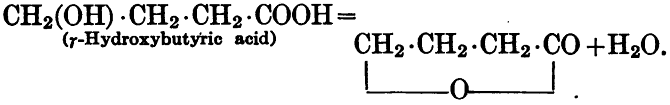
is pathologically of importance, since it may occur in blood or urine, especially in the disease diabetes. It is lævorotatory.

It will be noticed that the ketone acid *acetoacetic acid* (β-ketobutyric acid) corresponds to the above alcohol acids, just as ketones correspond to secondary alcohols (see also p. 140):

$CH_3\cdot CHOH\cdot CH_2\cdot COOH$ (*cf.* $CH_3\cdot CHOH\cdot CH_3$),
$CH_3\cdot CO\cdot CH_2\cdot COOH$ (*cf.* $CH_3\cdot CO\cdot CH_3$).

β-Hydroxyethylsulphonic acid (isethionic acid), $CH_2(OH)\cdot CH_2\cdot SO_3H$, enters into the synthesis of taurin (see p. 186).

γ-Hydroxy-acids are very unstable. They readily split off water to form anhydrides called **lactones,** thus:



$$CH_2(OH)\cdot CH_2\cdot CH_2\cdot COOH = \underbrace{CH_2\cdot CH_2\cdot CH_2\cdot CO}_{O} + H_2O.$$

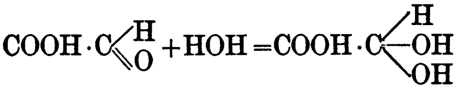
(γ-Hydroxybutyric acid) (Butyrolactone)

The carbon chain is closed by a linking through oxygen. It is not a typical closed chain, however. When boiled with caustic alkalies the lactones form salts of the corresponding hydroxy-acids; thus lactones give a "saponification value." This fact must be borne in mind in examining unknown substances supposed to be fats or waxes.

Dihydroxymonobasic acids are illustrated by **glyceric acid,**

$$\begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ COOH. \end{array}$$

Glyoxylic acid, which has been previously mentioned (p. 142), while classed as an aldehydic acid, is really a dihydroxy-acid, because it holds a molecule of water inseparable from it (*cf.* chloral hydrate):

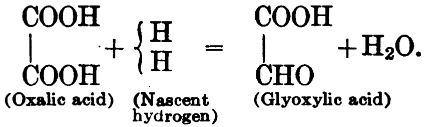


$$COOH\cdot C\begin{array}{l} \diagup H \\ \diagdown\!\!\diagdown O \end{array} + HOH = COOH\cdot C\begin{array}{l} \diagup H \\ - OH \\ \diagdown OH \end{array}$$

or

$$CH(OH)_2\cdot COOH.$$

Experiments. (1) To a strong solution of oxalic acid add some sodium amalgam (prepared by adding metallic sodium, a little piece at a time, to mercury until the latter loses its fluid condition); when evolution of gas has ceased, filter. The filtrate is a dilute solution of glyoxylic acid:



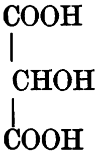
$$\underset{\text{(Oxalic acid)}}{\begin{array}{l}\mathrm{COOH}\\ |\\ \mathrm{COOH}\end{array}} + \underset{\text{(Nascent hydrogen)}}{\left\{\begin{array}{l}\mathrm{H}\\ \mathrm{H}\end{array}\right.} = \underset{\text{(Glyoxylic acid)}}{\begin{array}{l}\mathrm{COOH}\\ |\\ \mathrm{CHO}\end{array}} + H_2O.$$

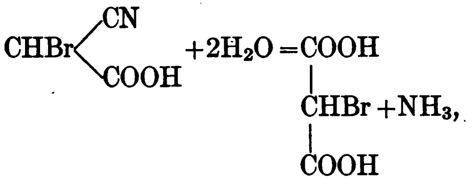
(2) To 5 c.c. of albumin solution (egg-white solution) add 5 c.c. of the glyoxylic acid solution, then 5 c.c. of concentrated H_2SO_4; mix and heat gradually; a bluish-violet colour is obtained, due to tryptophan contained in the proteid molecule. Most proteids give this test.

An example of a **trihydroxy-acid** is **cholic** or cholalic acid, $C_{20}H_{31}(CHOH)\cdot(CH_2OH)_2\cdot COOH$. This is important physiologically, being contained, in combination with glycin and with taurin, in bile.

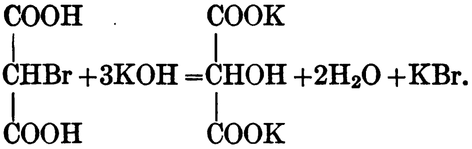
Glycuronic acid is an **aldehydic tetrahydroxy-acid,** $CHO\cdot(CHOH)_4\cdot COOH$, and is of physiological importance. It may occur in the urine, particularly after the administration of certain drugs (e.g., chloral hydrate), which are excreted in a glycuronic-acid combination. It is closely related to monosaccharides, having the same formula as dextrose, except for the change of the CH_2OH group of the latter to COOH. The free acid and some of its combinations reduce alkaline copper solutions (like other aldehydes). This may cause a mistake in urine examination. It is not fermentable. It gives the pentose reactions (see p. 211).

Monohydroxydibasic Acids.

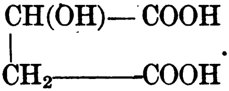
Tartronic acid,  $\begin{array}{l}COOH\\ |\\ CHOH\\ |\\ COOH\end{array}$, takes part in the physiological synthesis of uric acid (see uric acid, p. 202). It can be prepared by hydrolysis of bromcyanacetic acid,



$$CHBr\begin{array}{l}\diagup CN\\ \diagdown COOH\end{array}+2H_2O=\begin{array}{l}COOH\\ |\\ CHBr\\ |\\ COOH\end{array}+NH_3,$$



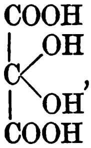
$$\begin{array}{l}COOH\\ |\\ CHBr\\ |\\ COOH\end{array}+3KOH=\begin{array}{l}COOK\\ |\\ CHOH\\ |\\ COOK\end{array}+2H_2O+KBr.$$

Malic acid is hydroxysuccinic acid,  $\begin{array}{l}CH(OH)—COOH\\ |\\ CH_2——COOH\end{array}$.

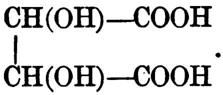
It is contained in sour fruits, e.g., apples and cherries.

Agaric or **agaricinic acid** is also a monohydroxydibasic acid, $C_{14}H_{27}(OH)(COOH)_2$. It is used as a medicine.

Dihydroxydibasic Acids.

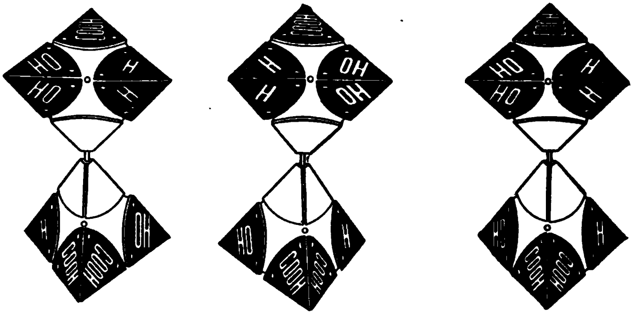
Mesoxalic acid,  $\begin{array}{l}COOH\\ |\\ C\begin{array}{l}\diagup OH\\ \diagdown OH\end{array}\\ |\\ COOH\end{array}$, is the third exception to the rule that two hydroxyls cannot be attached to the same carbon atom, chloral hydrate and glyoxylic acid being the other two exceptions.

Tartaric acid is dihydroxysuccinic acid,



$$\begin{array}{l}\mathrm{CH(OH)—COOH}\\ |\\ \mathrm{CH(OH)—COOH}\end{array}.$$

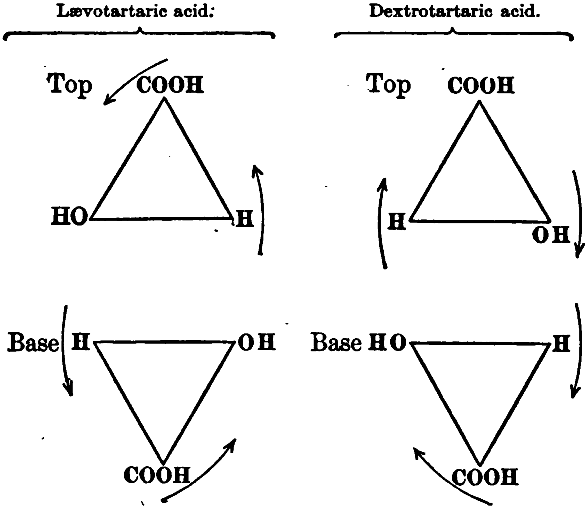
Here there are *two* asymmetric carbon atoms (see p. 168) in the molecule. This fact causes a species of stereoisomerism which is more difficult to understand than that of lactic acid. With the aid of models it can be clearly understood. Arrange pairs of tetrahedra as shown in the diagram.



Lævotartaric acid. **Dextrotartaric acid.** **Mesotartaric acid.**

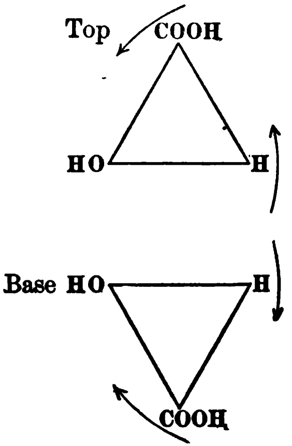
FIG. 22.

It will be noticed in the case of *dextro- and lævo-tartaric acids* that like groups, OH and OH, H and H, COOH and COOH, are connected by straight lines and are on opposite sides of a line connecting the centres of the tetrahedra. Notice, further, the order of arrangement of the groups on the top and on the base, for if the upper horizontal plane is lowered to approximate the plane of the base, the groups are found to have the same relative positions in both· this is represented also as follows:



Place the lævotartaric model before a mirror; the image corresponds to dextrotartaric acid.

Racemic tartaric acid is a mixture of equal quantities of dextro- and lævo-tartaric acids (*cf.* racemic lactic acid). There is, however, another inactive tartaric acid which cannot be separated into optically active acids. This is *mesotartaric acid.* By studying the diagram above, or a model, it will be seen that the neutralization of optical properties is an inner molecular one, for the arrangement of the groups on the top corresponds to that of lævotartaric acid, while the arrangement at the base corresponds to that of dextrotartaric.[1]



Ordinary tartaric acid is dextrorotatory. It is contained in grape-juice as potassium bitartrate or acid tartrate, $HOOC(CHOH)_2COOK$. When wine is produced this salt separates out, because of its relative insolubility in dilute alcohol. This crude tartar, or argol, is called cream of tartar when purified. It is used in the manufacture of the best baking-powders. Baking-powder is a mixture of sodium bicarbonate and some acid salt, which on being dissolved liberates carbon dioxide from the bicarbonate. Tartaric acid is obtained from potassium bitartrate by precipitation of calcium tartrate, from which the acid is liberated by using the proper amount of dilute sulphuric acid. It forms large crystals, melting at 170°. On heating further it turns brown and gives off an odour like caramel. It is very soluble.

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[1] It will further be noted that an acid of this variety is not possible in the case of lactic acid.

Dextrotartaric acid can be converted into racemic acid by boiling with an excess of strong sodium hydroxide solution. The two methods given for separating racemic lactic acid into the active acids are applicable also to racemic tartaric acid. Pasteur discovered a third method which is very interesting. By slow evaporation (below 28°) of a solution of sodium ammonium racemate two classes of crystals can be obtained, which from their appearance might be called right-handed and left-handed crystals (see Fig. 23).

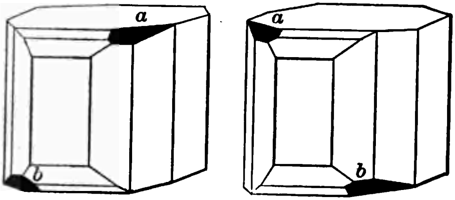
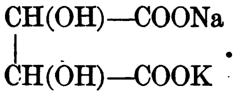


FIG. 23.

The crystals are mirror-images of one another. These can be picked out mechanically; one set furnishes dextrotartaric acid, the other lævotartaric acid.

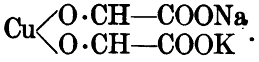
Rochelle salts is sodium potassium tartrate,



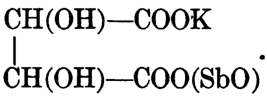
$$\begin{array}{l}\text{CH(OH)—COONa}\\ |\\ \text{CH(OH)—COOK}\end{array}$$

This has the power of holding $Cu(OH)_2$ in solution.

The copper is said to be held in the following combination (see Fehling's solution, p. 9):



Tartar emetic is potassium antimonyl tartrate,



$$\begin{array}{l} CH(OH)—COOK \\ | \\ CH(OH)—COO(SbO) \end{array}.$$

EXPERIMENTS. (1) Heat some tartaric acid in a test-tube, stirring it with a thermometer. Note the melting-point. Remove the thermometer and continue heating. The acid turns brown and emits an odour like scorched sugar.[1]

(2) Prepare tartar emetic. Dissolve 1 gm. of tartaric acid in 2 c.c. of water with heat, neutralize with strong KOH solution, add another gram of the acid. Boil and add water gradually until the precipitate redissolves. Now add Sb_2O_3 in excess, stirring vigorously. Filter and test the filtrate for antimony with H_2S.

(3) After reading over a description of the polariscope[2] and its manipulation, determine the rotary power of a strong solution of tartaric acid and of an equimolecular solution of sodium tartrate.

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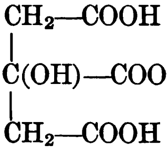
[1] Certain other acids act in the same way, particularly citric, malic, tannic, and gallic.

[2] A good description can be found in *Cohen's* Practical Organic Chemistry, also in Practical Physiology by *Beddard, Macleod*, etc.

Monohydroxytribasic Acids.



Citric acid, $\begin{array}{l} CH_2\text{—}COOH \\ | \\ C(OH)\text{—}COOH \\ | \\ CH_2\text{—}COOH \end{array}$, is present in currants, gooseberries, and lemons. It forms large crystals and is quite soluble. Citrates are valuable medicines (diuretics).

CHAPTER XVIII.

MIXED COMPOUNDS (*Continued*). AMIDO ACIDS AND ACID AMIDES.

AMIDO ACIDS.

Amido or amino acids are acids containing an NH_2 or amido group. Corresponding to monochloracetic acid, $CH_2Cl \cdot COOH$, is aminoacetic acid, $CH_2NH_2 \cdot COOH$.

The simplest amino acid is aminoformic acid, $NH_2 \cdot COOH$, called **carbamic acid.** The free acid is unknown. The salts are unstable, showing a decided tendency to become converted into carbonates. Ammonium carbamate is of considerable importance in physiology, because it is believed to be one of the forerunners of urea. It can be changed into urea by heating it in a sealed tube at a temperature of 135°–140°:

$$\underset{\text{(Ammonium carbamate)}}{NH_2 \cdot COONH_4} = \underset{\text{(Urea)}}{NH_2 \cdot CO \cdot NH_2} + H_2O.$$

EXPERIMENT. Prepare ammonium carbamate by bubbling dry CO_2[1] and dry NH_3 simultaneously into alcohol contained in a cylinder or graduate. Secure the dry NH_3 as previously described (see p. 106). Dry the CO_2 by bubbling it through H_2SO_4. When a considerable quantity of crystals has been produced, stop the process. Filter off the alcohol; press the crystals between filter-paper. To test the carbamate, dissolve some of the crystals in 5 c.c. of distilled water which has been cooled to 0°; immediately add some $CaCl_2$ solution which has been similarly cooled. No reaction is apparent because calcium carbamate in solution is stable at very low temperatures. Now warm the solution; the carbamate decomposes and a heavy precipitate of calcium carbonate appears. Leave the rest of the crystals exposed to the air several days; a small amount of a white powder (NH_4HCO_3) is obtained:

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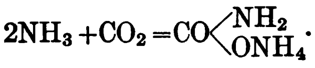
[1] CO_2 is obtained by putting marble chips into a bottle or generator and adding HCl by a dropping funnel.



$$2NH_3 + CO_2 = CO\left\langle\begin{matrix}NH_2\\ ONH_4\end{matrix}\right. .$$

Ethyl carbamate, or **urethane**, $NH_2 \cdot COOC_2H_5$, is used as a hypnotic.

Amino acids may be obtained by treating a halogen fatty acid with ammonia, thus:

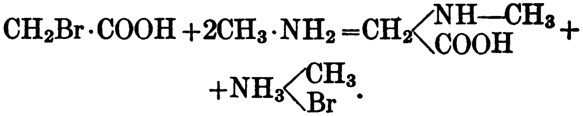
$$\underset{\text{(Monochloracetic acid)}}{H_2N\boxed{H + Cl}H_2C \cdot COOH} = \underset{\text{(Aminoacetic acid)}}{NH_2 \cdot CH_2 \cdot COOH} + HCl.$$

They can also be obtained by decomposing proteids by means of acids, alkalies, or hydrolytic ferments.

All the amino-acids that are considered in this chapter are of great importance in physiology.

Glycocoll (glycin) is aminoacetic acid, $CH_2\begin{matrix}\diagup NH_2\\ \text{——}COOH\end{matrix}$. It can be produced from glue (or gelatin) by boiling with dilute sulphuric acid or baryta water. In the animal body it combines with benzoic acid to form hippuric acid (see p. 277), and with cholic acid to form one of the bile acids, glycocholic acid.

Methyl glycocoll, $CH_2{<}\begin{matrix}NH\cdot CH_3\\ COOH\end{matrix}$, is called *sarcosin.* It can be synthesized from monobromacetic acid and methylamine:



$$CH_2Br\cdot COOH + 2CH_3\cdot NH_2 = CH_2{<}\begin{matrix}NH\text{—}CH_3\\ COOH\end{matrix} + \\ + NH_3{<}\begin{matrix}CH_3\\ Br\end{matrix}.$$

It is a product of decomposition of kreatin and of caffeine.

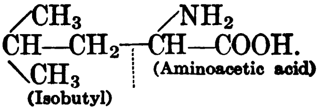
Alanin, $CH_3\cdot CH\cdot NH_2\cdot COOH$, is α-aminopropionic acid. It can be made from α-chlorpropionic acid by treatment with ammonia. It is isomeric with sarcosin.

Serin is hydroxyalanin, $CH_2OH\cdot CHNH_2\cdot COOH$.

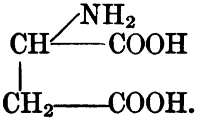
Aminovaleric acid has the formula

$$CH_3\cdot CH_2\cdot CH_2\cdot CHNH_2\cdot COOH.$$

Leucin is α-aminoisobutylacetic acid,



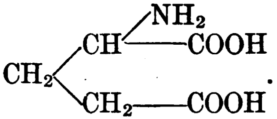
This may occur in the urine in certain diseases. It is a decomposition product of proteid, being an important end product of tryptic digestion.



$$\begin{array}{l}\mathrm{CH}\begin{array}{l}\diagup\mathrm{NH_2}\\ \text{—}\mathrm{COOH}\end{array}\\ \ | \\ \mathrm{CH_2\text{——}COOH}\end{array}$$

Aspartic acid is aminosuccinic acid, $CH(NH_2)COOH \cdot CH_2$——$COOH$. It is obtainable from asparagin and from proteid.

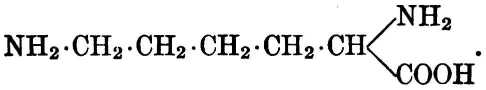
Glutaminic acid is α-aminoglutaric acid,



$$\mathrm{CH_2}\begin{array}{l}\diagup\mathrm{CH}\begin{array}{l}\diagup\mathrm{NH_2}\\ \text{——}\mathrm{COOH}\end{array}\\ \diagdown\mathrm{CH_2\text{——}COOH}\end{array}.$$

Gelatin and caseinogen can be split up so as to furnish a considerable proportion of this acid.

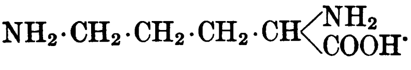
Lysin is $\alpha\epsilon$-diaminocaproic acid,



$$\mathrm{NH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH}\begin{array}{l}\diagup\mathrm{NH_2}\\ \diagdown\mathrm{COOH}\end{array}.$$

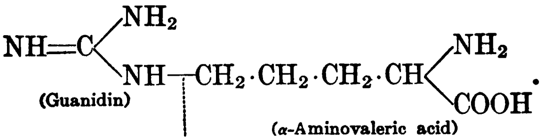
It is one of the products of proteid when boiled with mineral acid.

Ornithin is $\alpha\delta$-diaminovaleric acid,



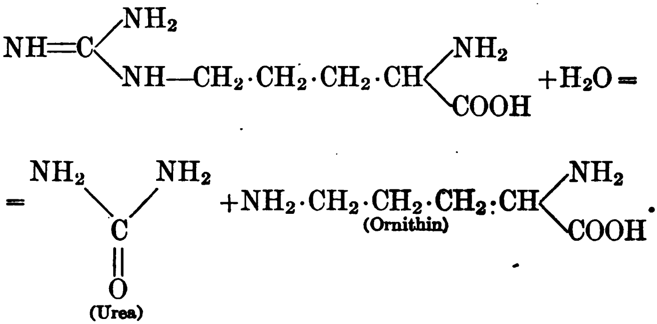
$$\mathrm{NH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH}\begin{array}{l}\diagup\mathrm{NH_2}\\ \diagdown\mathrm{COOH}\end{array}.$$

Arginin is related to ornithin, being guanidin-α-aminovaleric acid,



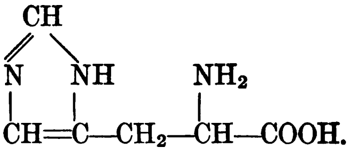
$$\mathrm{NH{=}C}\begin{array}{l}\diagup\mathrm{NH_2}\\ \diagdown\mathrm{NH}\text{—}\mathrm{CH_2\cdot CH_2\cdot CH_2\cdot CH}\begin{array}{l}\diagup\mathrm{NH_2}\\ \diagdown\mathrm{COOH}\end{array}\end{array}.$$

It can be hydrolyzed to urea and ornithin, thus:



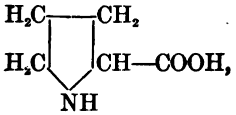
A ferment, arginase, found mainly in the liver, can also bring about this hydrolysis.

Lysin and arginin are called **hexone bases** (hexone refers to their possessing six carbon atoms in the molecule). Another hexone base is histidin, $C_6H_9N_3O_2$, probably



It is now believed that these hexone bases are present in combination in all proteid molecules. The simplest proteids, *protamines*, seem to contain practically nothing besides hexone bases and in some cases amino acids.

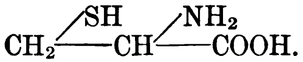
It seems advisable to mention in this place two derivatives of pyrrolidine (see under alkaloids, p. 328), because they are obtained together with the above amino acids as decomposition products of proteids. They are *prolin* or α-pyrrolidine-carboxylic acid,



and hydroxy-α-pyrrolidine-carboxylic acid.

SULPHUR DERIVATIVES OF AMINO ACIDS.

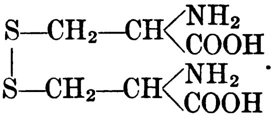
Cystein is α-amino-β-thiolactic acid:



$$CH_2\overset{SH}{\diagup}\!\!—CH\overset{NH_2}{\diagup}\!\!—COOH.$$

Two molecules combine to form one molecule of cystin.

Cystin has the formula

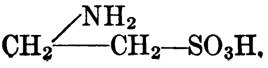


$$\begin{array}{l} S—CH_2—CH\begin{cases}NH_2\\COOH\end{cases}\\ \mid \\ S—CH_2—CH\begin{cases}NH_2\\COOH\end{cases}\end{array}.$$

Both cystein and cystin occur as decomposition products of proteids.

Cystin crystals may occur in pathological urine. Cystin from urine has a slightly different linking of the S from that in the above formula. Reduction of cystin gives cystein as its product.

Taurin is β-aminoethylsulphonic acid,



$$CH_2\overset{NH_2}{\diagup}\!\!—CH_2—SO_3H,$$

It is found in bile combined with cholic acid as taurocholic acid. It has been synthesized from β-hydroxyethylsulphonic acid (see p. 171), as indicated by the following equations:

$$CH_2(OH)\cdot CH_2\cdot SO_3H + 2PCl_5 =$$

$$= CH_2Cl\cdot CH_2SO_2Cl + 2POCl_3 + 2HCl.$$

(Chlorethylsulphon chloride)

$$CH_2Cl\cdot CH_2\cdot SO_2Cl + H_2O = CH_2Cl\cdot CH_2\cdot SO_3H + HCl.$$

(Chlorethylsulphonic acid)

$$CH_2Cl\cdot CH_2\cdot SO_3H + 2NH_3 =$$

$$= CH_2NH_2\cdot CH_2\cdot SO_3H + NH_4Cl.$$

(Taurin)

ACID AMIDES.

The next group of amido compounds to be considered is that of the acid amides. Just as there are acid chlorides, e.g., acetyl chloride, $CH_3\cdot COCl$, so there are acid amides, NH_2 occupying the position of Cl, as acetamide, $CH_3\cdot CONH_2$.

Acid amides may be made in several ways:

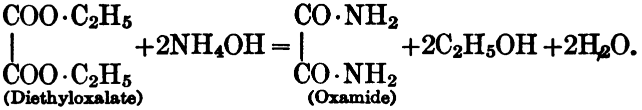
(1) By treating an acid chloride with ammonia:

$$CH_3\cdot CO\boxed{Cl + H}NH_2 = CH_3\cdot CONH_2 + HCl.$$

(2) By heating an acid in an atmosphere of ammonia while constantly bubbling dry ammonia gas into the acid:

$$CH_3\cdot CO\boxed{OH + H}NH_2 = CH_3\cdot CONH_2 + H_2O.$$

(3) By treating an ester with ammonia:



$$\underset{\text{(Diethyloxalate)}}{\begin{array}{l}COO\cdot C_2H_5\\ |\\ COO\cdot C_2H_5\end{array}} + 2NH_4OH = \underset{\text{(Oxamide)}}{\begin{array}{l}CO\cdot NH_2\\ |\\ CO\cdot NH_2\end{array}} + 2C_2H_5OH + 2H_2O.$$

(4) By heating the ammonium salt of the acid, generally in a sealed tube:

$$\underset{\text{(Ammonium acetate)}}{CH_3\cdot COONH_4} = \underset{\text{(Acetamide)}}{CH_3\cdot CONH_2} + H_2O.$$

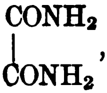
Formamide, $H\cdot CONH_2$, is a liquid. The other acid amides are solid crystalline substances.

Acetamide, $CH_3\cdot CONH_2$, is prepared by the fourth method given above (see exp.). It forms colourless crystals, which melt at 82° and distil at 223°. It generally has a mouse-like odour, due to slight admixture of impurities. Heating with phosphorus pentoxide converts it into methyl cyanide (see p. 155).

EXPERIMENT. To 40 gm. of glacial acetic acid heated to 40°–50° on a water bath, add powdered ammonium carbonate (about 55 gm.) until a drop diluted with a few cubic centimetres of water shows a weak alkaline reaction to litmus. Now heat to 80°–90° on a boiling water bath until a drop diluted with water shows a slightly acid reaction. Pour the mass while hot into a Volhard tube or bomb-tube through a hot funnel (so as not to smear the walls of the tube). With a strip of filter-paper remove any of the substance that may be adhering to the upper eight inches of the tube.

Seal the tube carefully. The sealing of bomb-tubes requires practice. Experiment first with waste pieces of tubing. First cover the tube with soot in a smoky flame at the point where it is to be sealed. Increase the heat gradually, then begin with a large blast flame. When the soot is burned off, decrease the size of the flame, increasing the force of the blast. Keep rotating the tube, and when it softens do not draw it out, but make the tube sink in by the force of the blast. In this way the thickness of the wall is preserved. When the calibre of the tube has become very small, the tube can be quickly drawn out and sealed off. A tapering tip is the best. Heat the tip in the flame until rounded. Keep the hot end of the tube in a cold smoky flame until a deposit of soot is obtained. Let it cool slowly.

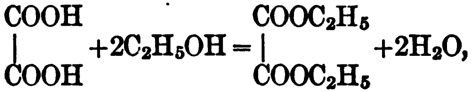
Heat the tube in a bomb-furnace for five hours at 220°–230°. Open the tube by making a scratch-mark with a file on the tip; wrap the tube in a heavy towel; put the tip into the blast-flame, when it will snap off. Sometimes there is a high pressure of gases in a bomb-tube, so that it may fly to pieces as soon as the pressure is suddenly relieved. Break off the end of the tube; remove the acetamide and transfer it to a distilling flask. Distil, reject the distillate coming over below 130°, then change to a wide tube (air-condenser) in the place of the Liebig condenser. Collect the fraction distilling between 180° and 230° in a beaker. Cool it with ice-water until crystals form; if necessary, scratch the wall of the beaker with the sharp end of a glass rod (see p. 8). Dry the crystals by pressing them on a porous plate.

Oxamide, 

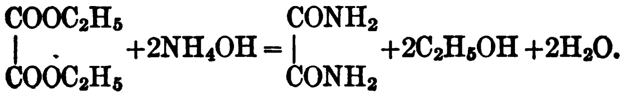
$$\begin{array}{l} CONH_2 \\ | \\ CONH_2 \end{array}$$

, is prepared by the third method.

EXPERIMENT. Connect two flasks with a glass tube bent at a right angle at each end. In the second flask the tube is long enough to almost reach the bottom. Into each flask put 50 c.c. of absolute alcohol. Into the second flask put also 50 gm. of oxalic acid from which the water of crystallization has been driven off by heating in an oven at 100°. The first flask is supported on wire gauze, while the second is placed in an oil-bath. Place a thermometer in the oil. Connect the second flask with a condenser. Heat the oil-bath to 100°, then begin heating the flask containing only alcohol. While the alcohol-vapour is passing over, allow the temperature of the oil-bath to rise slowly to 125°–130°. When most of the alcohol has disappeared from flask number one, disconnect this flask and remove the flame. The distillate and the residue in flask number two both contain diethyl oxalate. Treat each with strong ammonium hydroxide. A white precipitate of oxamide is obtained. Filter and wash the precipitate thoroughly. Save a sample. Put some oxamide into a test-tube, add strong alkali, and boil, noting the evolution of ammonia. Take another portion in a test-tube, treat with cold NaOH, and add very dilute copper sulphate solution a drop at a time until a reddish or violet colour appears (biuret reaction, see p. 193):



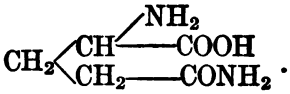
$$\begin{array}{l}COOH\\ |\\ COOH\end{array} + 2C_2H_5OH = \begin{array}{l}COOC_2H_5\\ |\\ COOC_2H_5\end{array} + 2H_2O,$$



$$\begin{array}{l}COOC_2H_5\\ |\\ COOC_2H_5\end{array} + 2NH_4OH = \begin{array}{l}CONH_2\\ |\\ CONH_2\end{array} + 2C_2H_5OH + 2H_2O.$$

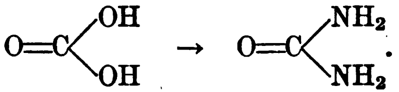
Asparagin is the amide of aspartic acid, its formula being $\begin{array}{l} CH_2\text{—}CONH_2 \\ | \\ CH(NH_2)\text{—}COOH \end{array}$. It is found in many vegetables, particularly asparagus, peas, beans, beets, and wheat.

Glutamin is the amide of glutaminic acid, having the formula



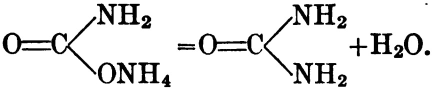
$$CH_2\begin{cases} CH\begin{matrix} NH_2 \\ COOH \end{matrix} \\ CH_2\text{——}CONH_2 \end{cases}.$$

The most important acid amide of all is *carbamide*. **Urea** (carbamide), $NH_2 \cdot CONH_2$, is the acid amide of carbamic acid. It is also the diamide of carbonic acid:



$$O{=}C\begin{matrix} OH \\ OH \end{matrix} \rightarrow O{=}C\begin{matrix} NH_2 \\ NH_2 \end{matrix}.$$

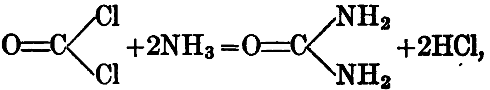
The relationship of urea to carbamic acid is shown by its preparation from ammonium carbamate by heating in a sealed tube at a temperature of 135°:



$$O{=}C\begin{matrix} NH_2 \\ ONH_4 \end{matrix} = O{=}C\begin{matrix} NH_2 \\ NH_2 \end{matrix} + H_2O.$$

(Ammonium carbamate) (Urea)

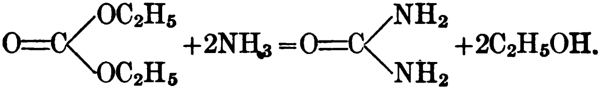
Its relationship to carbonic acid is evidenced by its production from carbonyl chloride and ammonia:



$$O{=}C\begin{matrix} Cl \\ Cl \end{matrix} + 2NH_3 = O{=}C\begin{matrix} NH_2 \\ NH_2 \end{matrix} + 2HCl,$$

(Carbonyl chloride)

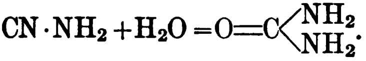
also from ethyl carbonate and ammonia:



$$O=C\begin{matrix}OC_2H_5\\ OC_2H_5\end{matrix}+2NH_3=O=C\begin{matrix}NH_2\\ NH_2\end{matrix}+2C_2H_5OH.$$

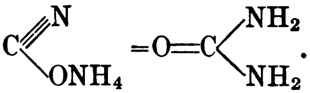
(Ethy carbonate)

That it bears a relationship to cyanic acid, $HCNO$, and its amide cyanamide, $N\equiv C-NH_2$, is proven by its preparation from both of these. By hydrolysis cyanamide is converted into urea:



$$CN\cdot NH_2+H_2O=O=C\begin{matrix}NH_2\\ NH_2\end{matrix}.$$

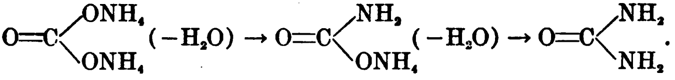
Mere evaporation of a solution of ammonium cyanate is sufficient to convert the salt into urea (see exp.):



$$C\begin{matrix}\equiv N\\ -ONH_4\end{matrix}=O=C\begin{matrix}NH_2\\ NH_2\end{matrix}.$$

(Ammonium cyanate)

Physiologists have advocated three main hypotheses as to the origin of urea in the animal body, corresponding to the above methods of synthesis, namely, that it is derived from (1) ammonium carbonate, (2) from ammonium carbamate, or (3) from ammonium cyanate. The question is still unsettled, but at present it seems most likely that the derivation of urea is as follows: Ammonia enters the blood of the portal venous system partly as the result of metabolism of active digestive glands and partly as the result of fermentative disintegration of the proteids of the food. In the presence of the large amount of carbonic acid in the blood, ammonium carbonate and carbamate are formed in accordance with the laws of mass action; both of these are then converted in the liver into urea by a process of anhydrolysis:



$$O{=}C\begin{matrix}\diagup ONH_4\\ \diagdown ONH_4\end{matrix}(-H_2O)\rightarrow O{=}C\begin{matrix}\diagup NH_2\\ \diagdown ONH_4\end{matrix}(-H_2O)\rightarrow O{=}C\begin{matrix}\diagup NH_2\\ \diagdown NH_2\end{matrix}.$$

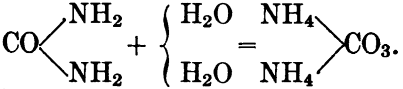
(Ammonium carbonate) (Ammonium carbamate) (Urea)

It seems questionable, however, whether any considerable quantity of ammonia is produced from the proteids of the body-tissues. General tissue metabolism probably gives rise to monoamino-acids (as glycocoll, leucin, and aspartic acid) and arginin, all of which are convertible into urea (even as a laboratory experiment). In the case of arginin this is accomplished by a ferment, arginase, which is present in many organs. In the case of monoamino-acids it may be that they are converted by ferments into ammonia, for the presence of ferments possessing that power has been demonstrated in many organs, and that then the ammonia becomes ammonium carbonate and carbamate, and is changed to urea.

It is possible that diamino-acids are predecessors also of urea, since it has been found that one of them, ornithin (the other product of the hydrolysis of arginin besides urea), increases urea excretion when it is injected intravenously. Diamino-acids have not yet been converted into urea in the laboratory.

Urine contains a large quantity of urea, 20 to 30 gm. of urea being excreted in the urine of man in twenty-four hours on a mixed diet. It crystallizes in colourless needles or rhombic prisms. It melts at 132° (corrected melting-point is 132.6°). It is very soluble in water and hot alcohol, less soluble in cold alcohol.

Bacterial fermentation of urine converts urea into ammonium carbonate, hence the ammoniacal odour of decomposed urine. Boiling with alkalies or acids or superheating with water accomplishes a similar hydrolysis:



$$CO\begin{matrix}\diagup NH_2 \\ \diagdown NH_2\end{matrix} + \left\{\begin{matrix} H_2O \\ H_2O \end{matrix}\right. = \begin{matrix} NH_4\diagdown \\ NH_4\diagup \end{matrix}CO_3.$$

Of course by the action of alkali NH_3 is liberated from the $(NH_4)_2CO_3$, while by the action of acid CO_2 is liberated. This reaction is the basis of Bunsen's and Folin's methods of quantitative estimation of urea. Sodium hypochlorite and hypobromite decompose urea, liberating nitrogen:

$$CO(NH_2)_2 + 3NaBrO = N_2 + 3NaBr + CO_2 + 2H_2O.$$

This reaction is made use of in the usual clinical method for urea estimation. Nitrous acid also liberates free nitrogen (see p. 159):

$$CO(NH_2)_2 + 2HNO_2 = 2N_2 + CO_2 + 3H_2O.$$

When heated strongly, urea yields, among other substances, *biuret*, $NH_2 \cdot CO \cdot NH \cdot CO \cdot NH_2$, which gives a reddish-violet colour reaction with caustic soda or potash containing a trace of copper sulphate (*biuret reaction*). This reaction is given by proteids, by oxamide, in fact by all substances containing two groups of $CO \cdot NH_2$ linked together either directly (as in oxamide) or through a single nitrogen (as in biuret) or carbon atom $\left(\text{as in } CH_2\begin{matrix}\diagup CONH_2 \\ \diagdown CONH_2\end{matrix}\right)$, or through one or more $CO \cdot NH$ groups $\left(\text{as in } \begin{matrix} CO \cdot CONH_2 \\ | \\ NH \cdot CONH_2 \end{matrix}\right)$.

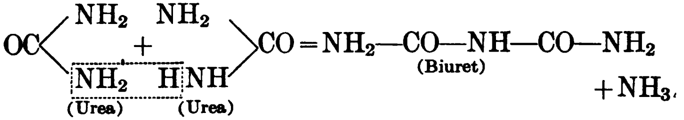
Urea acts as a weak base toward certain acids, the nitrate and oxalate being particularly characteristic salts. In the common method for extraction of urea from urine, it is precipitated from the urine (previously concentrated by evaporation) by treatment with nitric acid. The urea is liberated from the nitrate by treating the latter with barium carbonate.

EXPERIMENT. (1) Synthesize urea as follows: Heat 25 gm. of potassium cyanide in an iron dish until it begins to fuse (do this under a hood), then add gradually 70 gm. of red oxide of lead a little at a time, stirring in well. When the frothing ceases pour on to an iron plate. When it is cool powder the mass, separating out the metallic lead. Digest this crude cyanate for an hour with 100 c.c. of cool water. Filter through a plaited filter into an evaporating dish. Add to the filtrate 25 gm. of ammonium sulphate which has been dissolved in a small quantity of water. Evaporate to dryness on a water bath, stirring frequently to prevent crusting over. Cool the residue and powder it in a mortar. Transfer it to a small flask, add 100 c.c. of alcohol, attach to a reflux condenser, and boil for fifteen minutes. Filter off the hot alcohol into an evaporating dish. Use 25 c.c. more of alcohol in a similar manner. Evaporate the alcohol on a water bath to very small bulk. When cool, urea crystals should form. Test a few crystals or some of the solution as below.

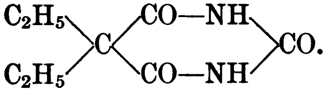
(2) *Urea tests.* (*a*) Put one drop of concentrated urea solution on a glass slide; mix with it one drop of colourless concentrated nitric acid. Place a cover-glass over the crystals and examine under a microscope.

(*b*) Lüdy's test. To a drop of dilute urea solution in an evaporating dish add about 1 c.c. of a slightly yellow solution of orthonitrobenzaldehyde in alcohol. Evaporate to dryness on a bath. Cool, add 5 c.c. of alcohol, warm slightly, and pour off the alcohol. Repeat this washing with alcohol until the alcohol is colourless and gives no colour reaction with an aqueous solution of phenylhydrazine hydrochloride. The yellowish-white residue is nitrobenzlidene diureide. Add about 3 c.c. of phenylhydrazine hydrochloride solution (use heat to dissolve it) and ten drops of 10% H_2SO_4. Heat to boiling; a red colour develops if urea is present. The test seems to be more successful with impure urea solutions than with pure urea.

(3) In a test-tube melt some dry urea, then heat gently for a minute while gas is being evolved. Cool; add 1 c.c. of water, then an equal amount of 20% NaOH solution, and finally a small drop of very dilute copper sulphate solution. A violet or pinkish colour is obtained. This is called the biuret reaction (see above):

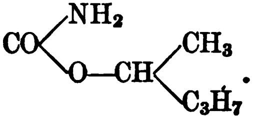


Veronal is a urea derivative, being diethylmalonylurea:



This is used as a hypnotic.

Another hypnotic related to urea is hedonal, which is really a carbamate similar to urethane. **Hedonal is** methylpropylcarbinolurethane:

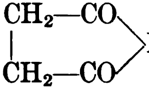


CHAPTER XIX.

MIXED COMPOUNDS (*Continued*). ACID IMIDES. COMPLEX AMIDO AND IMIDO COMPOUNDS, INCLUDING POLYPEPTIDES.

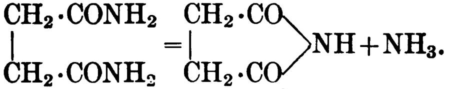
ACID IMIDES.

These contain the group NH; they are illustrated by succinimide,



$$\left.\begin{array}{l}CH_2-CO\\ |\\ CH_2-CO\end{array}\right\rangle NH.$$

They are formed from acid amides by loss of ammonia:

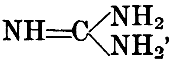


$$\begin{array}{l}CH_2 \cdot CONH_2\\ |\\ CH_2 \cdot CONH_2\end{array} = \left.\begin{array}{l}CH_2 \cdot CO\\ |\\ CH_2 \cdot CO\end{array}\right\rangle NH + NH_3.$$

(Succinamide) (Succinamide)

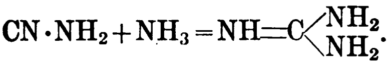
OTHER AMIDO AND IMIDO COMPOUNDS.

Guanidin,



$$NH{=}C\left\langle\begin{array}{l}NH_2\\ NH_2\end{array}\right.,$$

may be considered as an imido derivative of urea, and might be called imidocarbamide. It can be synthesized from cyanamide and ammonia:

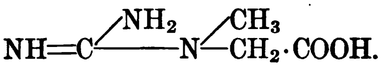


$$CN \cdot NH_2 + NH_3 = NH{=}C\left\langle\begin{array}{l}NH_2\\ NH_2\end{array}\right..$$

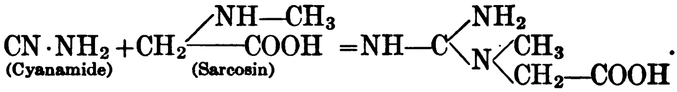
(Cayanamide) (Guanidin)

It is more strongly basic than urea, undoubtedly because of the changing of the carbonyl linking of urea for the naturally basic NH group. Of more importance are the derivatives of guanidin, namely, *kreatin* and *kreatinin.*

Kreatin is methylguanidinacetic acid,

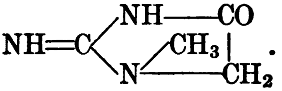


Kreatin can be synthesized from cyanamide and sarcosin:



Kreatin is present in considerable quantity in muscular tissue. It can be obtained from meat extract. Heating with baryta water converts it into urea, sarcosin and some other substances. Heating with dilute acid changes it to kreatinin. Recent work has shown, however, that only a certain fraction of the kreatin is thus converted into kreatinin. Only when the urine is alkaline is it excreted as kreatin in any appreciable quantity; it is generally eliminated as kreatinin.

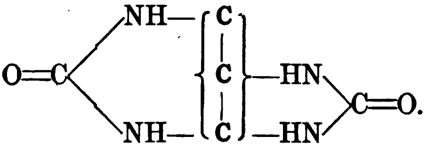
Kreatinin is kreatin less a molecule of water:



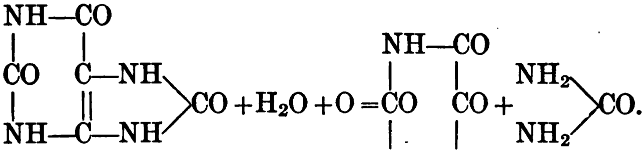
This is always present in normal human urine, about 1.5 gm. being excreted in twenty-four hours. The amount excreted when kreatin-containing food (flesh) is debarred from the diet seems to be a fixed quantity for each individual, no matter how much the total nitrogen content of the urine may vary.

Kreatinin crystallizes in monoclinic prisms. It is readily soluble. In alkaline solution it becomes converted, at least in part, into kreatin. It reduces Fehling's and other alkaline copper solutions, but it holds cuprous oxide in solution; on account of these properties it may mislead in testing for sugar if the urine is concentrated. An alkaline bismuth solution, however, is not reduced by kreatinin. Kreatinin is precipitated by mercuric chloride and by zinc chloride, these reagents entering into chemical union with the kreatinin.

Uric acid is a derivative of urea. In uric acid two molecules of urea unite together by linking to an intermediate carbon chain, each NH_2 group losing one hydrogen atom and becoming NH in order to effect the union:

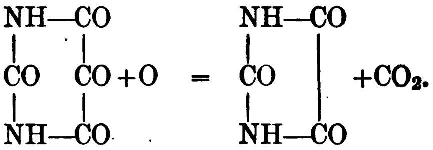


This is the skeleton of the uric acid formula. The presence of two urea molecules and of a carbon chain is shown by the nature of the decomposition products of uric acid resulting from oxidation and hydrolysis:

I. 

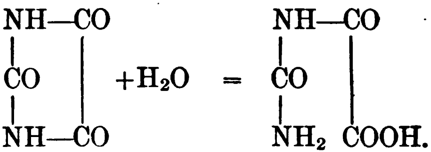
(Uric acid) [treated with cold HNO_3] (Alloxan) (Urea)

II.



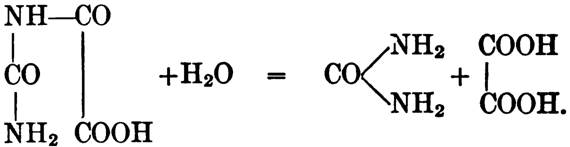
(Alloxan) [treated with warm HNO_3] (Parabanic acid)

III.

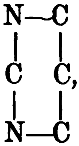


(Parabanic acid) [treated with alkali] (Oxaluric acid)

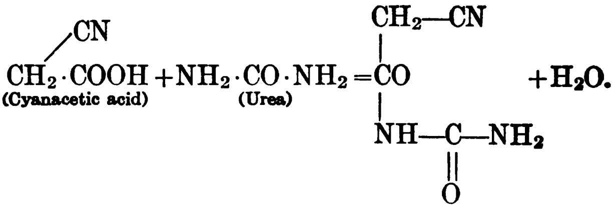
IV.



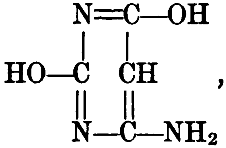
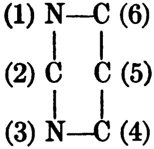
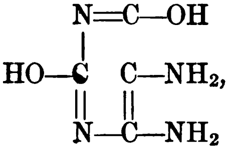
(Oxaluric acid) [boiled with water] (Urea) (Oxalic acid)

The presence of the pyrimidin ring,  in uric acid is shown by *Traube's synthesis*, which is as follows: Cyanacetic acid and urea are treated with $POCl_3$; the latter removes hydroxyl from the acid, and urea takes its place to form cyanacetyl urea:

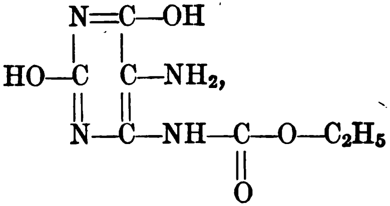
(1)



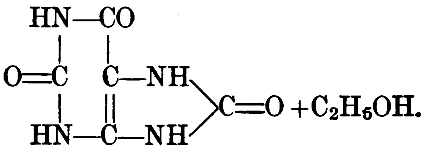
(Cyanacetic acid) (Urea) (Cyanacetyl urea)

Treating cyanacetyl urea with alkali causes a shifting within the molecule, resulting in the formation of the pyrimidin derivative, (2) , the positions in the pyrimidin ring being numbered thus: . The above compound is called 4-amino-2, 6-dihydroxypyrimidin. This is treated with HNO_2, giving (3) , 4, 5-diamino-2, 6-dihydroxypyrimidin, which when acted on by $CClOOC_2H_5 + KOH$ gives

(Ethyl chlorcarbonate)

(4) 

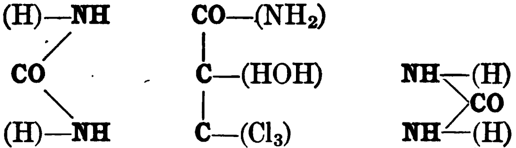
a pyrimidin derivative of urethane. The sodium salt of this is heated (dry) to 150°, then later to 180°–190°. Alcohol is split off, leaving uric acid (as sodium urate):

(5) 

(Uric acid)

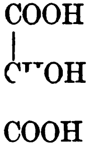
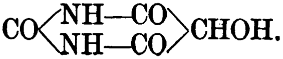
This synthesis conclusively proves the structure of uric acid.

Another interesting synthesis, because it is analogous to one which may occur in the animal body, is effected by heating together urea and trichlorlactamide:

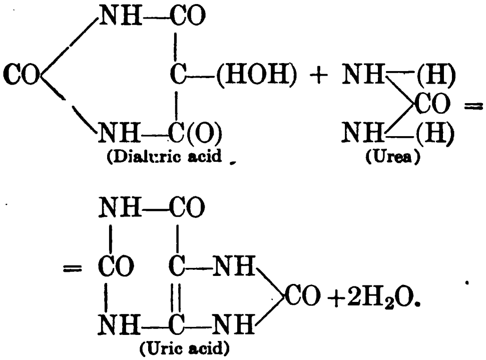


(Urea) (Trichlorlactamide) (Urea)

The groups in parenthesis do not enter into the uric acid molecule, but unite to form NH_4Cl, HCl, and H_2O.

It has been found that acids, e.g., lactic acid, which are convertible into tartronic acid,  $\begin{matrix}COOH\\|\\CHOH\\|\\COOH\end{matrix}$, can, under certain conditions, cause uric acid to be synthesized in the animal organism. Dialuric acid is first formed by attachment of a urea molecule,  $CO{<}\begin{matrix}NH-CO\\NH-CO\end{matrix}{>}CHOH$.

By the addition of another urea molecule to this, uric acid is produced:



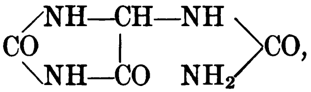
Uric acid has been synthesized by heating together glycocoll and urea. On the other hand, uric acid when heated in a sealed tube with HCl yields glycocoll.

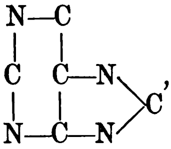
Uric acid acts as a weak dibasic acid, forming urates. It does not, however, play any part in the acid reaction of urine. It often crystallizes out as a reddish deposit from strongly acid urine. About 0.7 gm. is excreted daily by man. Pure uric acid is a colourless crystalline powder. It is almost insoluble in cold water and alcohol. Uric acid reduces Fehling's solution, but does not reduce an alkaline bismuth solution.

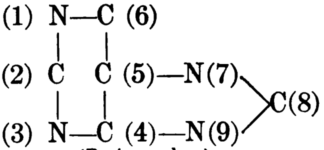
EXPERIMENT. (1) Add 5 c.c. of 20% HNO_3 to a little uric acid in an evaporating-dish; evaporate to dryness on a water-bath. Alloxantin is formed. To the residue add baryta water; a blue colour appears.

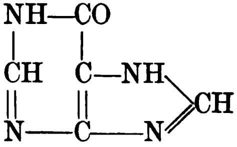
(2) Repeat the above, but instead of using baryta expose the residue to fumes of ammonia. A red colour

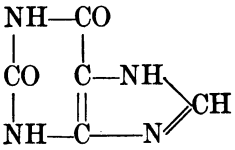
is obtained, due to murexide. This test is called the murexide test. If much ammonia is present in the air, the residue will be reddish because of the ammonia taken up.

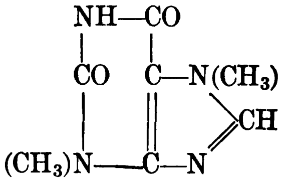
Allantoin,  results from careful oxidation of uric acid by potassium permanganate. It occurs in the urine of calves, and at times in human and in dogs' urine.

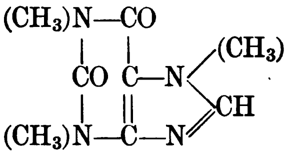
Purin. Uric acid and all the *purin bodies* contain the double-ring nucleus , which has been called purin. The main ring is the pyrimidin ring; purin therefore is pyrimidin with a urea residue attached as a secondary ring. The relationship of the purin bodies to purin is shown below:


(Purin nucleus)

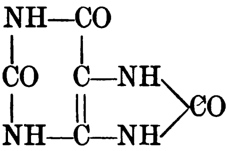

(Hypoxanthin)
(6-oxypurin)


(Xanthin
(2, 6-dioxypurin)

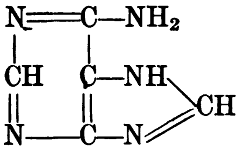

(Tneobromine, dimethylxanthin)
(3, 7-dimethyl-2, 6-dioxypurin)



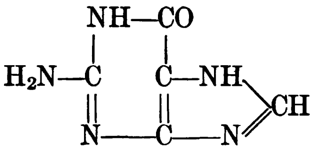
(Caffeine, theine, trimethylxanthin) (1, 3, 7-trimethyl-2, 6-dioxypurin)



(Uric acid) (2, 6, 8-trioxypurin)



(Adenin)
(6-aminopurin)



(Guanin)
(2-amino-6-oxypurin)

The purins are also called *alloxuric, xanthin,* or *nuclein* bodies.

Caffeine and theobromine when taken as food are excreted in the urine as xanthin and hypoxanthin. The other purins are excreted mainly as uric acid. It is believed by some that on a diet which is free of purin bodies the amount of purins excreted daily is a fixed quantity for each individual (*cf.* kreatinin).

Some of the purins, mainly xanthin and hypoxanthin, are found in muscle, and therefore in meat extract. *Beef tea* or a solution of *meat extract* contains as its organic constituents chiefly kreatin, purin bodies, and sarcolactic acid.

Theobromine (dimethylxanthin) is found in chocolate and cocoa. It is called an alkaloid (see p. 328).

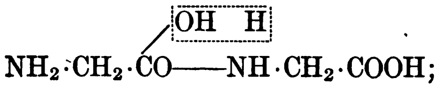
Caffeine or **theine** (trimethylxanthin) is the alkaloidal principle in tea and coffee. Both theobromine and caffeine are used as medicines.

Experiment. Try the murexide test (see p. 203) on a little caffeine. Repeat, substituting bromine water for HNO_3.

Leucomaine is a term applied to basic substances found in living animal tissues. The purin bodies and the kreatinin group of compounds are the chief leucomaines.

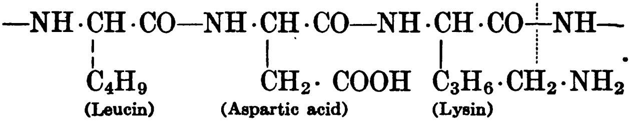
DIPEPTIDES AND POLYPEPTIDES.

Because of the fact that the decomposition products of proteids include amino-acids (as alanin, glycocoll, leucin, tyrosin, aspartic acid, etc.) and the hexone bases, it has been proposed to explain the structure of the proteid molecule as a chaining together of these amino bodies by means of the removal of OH of a carboxyl group of the one amido body and an H of the amido group of another (*cf.* formation of acid amides), thus:



$$\mathrm{NH_2\cdot CH_2\cdot CO}\overset{\boxed{\mathrm{OH\quad H}}}{\text{———}}\mathrm{NH\cdot CH_2\cdot COOH};$$

or a more complicated chain, as:



$$-NH\cdot\underset{\substack{C_4H_9\\ \text{(Leucin)}}}{CH}\cdot CO-NH\cdot\underset{\substack{CH_2\cdot COOH\\ \text{(Aspartic acid)}}}{CH}\cdot CO-NH\cdot\underset{\substack{C_3H_6\cdot CH_2\cdot NH_2\\ \text{(Lysin)}}}{CH}\cdot CO\,\vdots\,NH-$$

Of course the above is supposed to be only a part of the formula.

On the basis of this hypothesis the problem of the synthesis of proteid is now being vigorously attacked. Compounds have been synthesized in which two, three, and even up to twelve molecules have been made to combine in this manner; these synthetic bodies are called peptides.

If two molecules have united, the compound is a dipeptide; for example, glycylglycin,

$$NH_2\cdot CH_2\cdot CO-NH\cdot CH_2\cdot COOH.$$

Polypeptides are built up from more than two molecules; they include tripeptides (as diglycylglycin,

$$NH_2\cdot CH_2\cdot CO-NH\cdot CH_2\cdot CO-NH\cdot CH_2\cdot COOH),$$

tetrapeptides, pentapeptides, hexapeptides, a heptapeptide, octapeptide, dekapeptide and dodekapeptide,

$$C_4H_9\cdot CH(NH_2)\cdot CO\cdot(NH\cdot CH_2\cdot CO)_{10}-NH\cdot CH_2\cdot COOH.$$

This last peptide is leucyldekaglycylglycin, and has a molecular weight of 758.

A number of the peptides give the biuret reaction. Some of the polypeptides are said to bear certain resemblances to peptone in their reactions.

E. Fischer, who is doing such brilliant work in this line of synthesis, is inclined to doubt whether this comparatively simple method of linking is the only kind of linking existing in proteid molecules.

CHAPTER XX.

MIXED COMPOUNDS *(Continued)*.
CARBOHYDRATES AND GLUCOSIDES.

CARBOHYDRATES.

THIS last class of mixed compounds is of very great importance, since it includes sugars and starches. The name *carbo(n)hydrates* calls attention to the fact that the number of atoms of hydrogen and oxygen present in the molecule bear the same ratio to one another as in water;[1] therefore a general formula for carbohydrates may be given as $C_n(H_2O)_m$.

Formaldehyde, CH_2O might be considered as the simplest carbohydrate. but it is never classed as such. Mention has already been made (see p. 105) of the hypothesis that plants reduce carbonic acid to formaldehyde, and then condense many molecules of this to form first sugar, then starch.

All carbohydrates contain in their formulæ one or more primary alcohol (CH_2OH) groups, and most have at least one aldehyde (CHO) or ketone (CO) group and many secondary alcohol (CHOH) groups.

There are three classes of carbohydrates, namely,

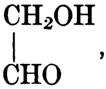
---

[1] It should be pointed out in this connection that the term hydrate as applied to alkalies is inaccurate, e.g., NaOH, sodium hydroxide, not a hydrate.

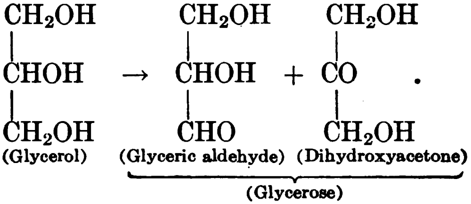
monosaccharides, *disaccharides*, and *polysaccharides*.[1] Monosaccharides are the simplest carbohydrates, containing but one aldehyde or ketone group. From the linking together of two monosaccharide molecules disaccharides result. Polysaccharides have complex molecules that can be resolved into many monosaccharide molecules.

MONOSACCHARIDES.

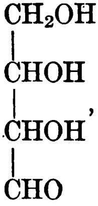
According to the number of carbon atoms present, monosaccharides are called dioses, trioses, tetroses, pentoses, hexoses, heptoses, octoses, and nonoses.

Glycol aldehyde,  $\begin{array}{l}CH_2OH\\|\\CHO\end{array}$, may be considered a **diose.**

Glycerose can be obtained by mild oxidation of glycerol (or lead glycerate); it is a mixture of an aldehyde and a ketone, and since each contains three carbon atoms, they are **trioses:**



$$\begin{array}{l}CH_2OH\\|\\CHOH\\|\\CH_2OH\\\text{(Glycerol)}\end{array} \rightarrow \underbrace{\begin{array}{l}CH_2OH\\|\\CHOH\\|\\CHO\\\text{(Glyceric aldehyde)}\end{array} + \begin{array}{l}CH_2OH\\|\\CO\\|\\CH_2OH\\\text{(Dihydroxyacetone)}\end{array}}_{\text{(Glycerose)}}.$$

Tetrose,  $\begin{array}{l}CH_2OH\\|\\CHOH\\|\\CHOH\\|\\CHO\end{array}$, can be obtained by polymerization of glycol aldehyde.

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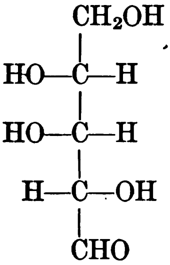
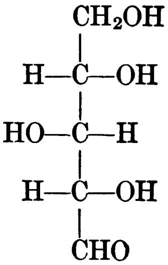
[1] These are also called monoses, bioses, and polyoses.

The chief **pentoses** are *d*-arabinose and *d*-xylose. The following formulæ represent their isomeric relation:



$$\begin{array}{c} CH_2OH \\ | \\ HO-C-H \\ | \\ HO-C-H \\ | \\ H-C-OH \\ | \\ CHO \end{array}$$

(*d*-Arabinose)



$$\begin{array}{c} CH_2OH \\ | \\ H-C-OH \\ | \\ HO-C-H \\ | \\ H-C-OH \\ | \\ CHO \end{array}$$

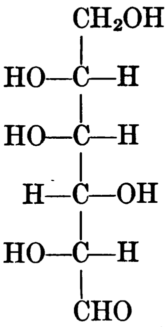
(*d*-Xylose)

Arabinose is obtainable by boiling gum-arabic with dilute acid. **Xylose** can be obtained by similar means from bran or wood. Racemic arabinose is sometimes present in the urine as an abnormal constituent.

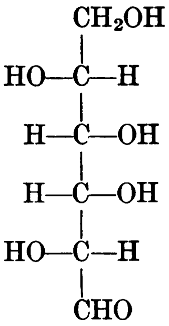
Both arabinose and xylose reduce Fehling's solution and form osazones with phenylhydrazine (the nature of the osazone reaction will be explained presently). Neither is fermented by pure yeast. They give certain colour reactions which will be illustrated in the experiment below.

EXPERIMENT. *Pentose test.* To 2 c.c. of water in a test-tube add 2 c.c. of HCl and warm. Add phloroglucin, a little at a time, as long as it dissolves. Now add 1 c.c. of arabinose solution, and heat until a red colour is obtained; examine at once with a small spectroscope, when an absorption band between the *d* and *e* lines will be seen. Heat until a precipitate forms, add some amyl alcohol, and shake—the alcohol becomes coloured and gives the same spectroscopic appearance as above.

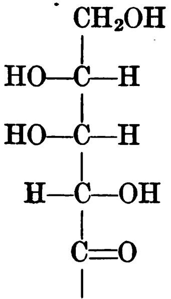
The **hexoses** are the sugars of prime importance. The chief ones are *dextrose, galactose,* and *lævulose;* the first two are aldehyde sugars or *aldoses,* while the last is a ketone sugar or *ketose:*



(Dextrose (glucose))

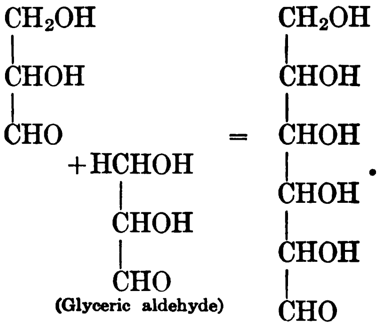


(Galactose)



(Lævulose (fructose))

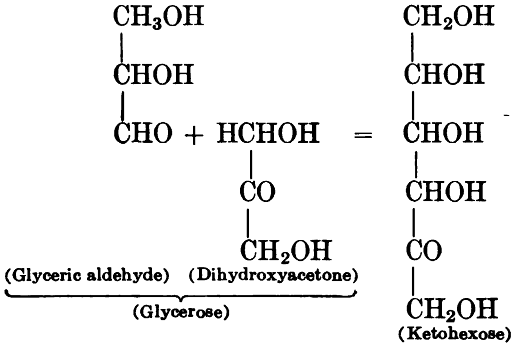
An aldose isomeric with dextrose and galactose can be made by condensation of two molecules of the triose, glyceric aldehyde:



(Glyceric aldehyde)

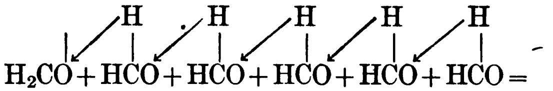
(Aldohexose)

In a similar manner condensation of the aldehyde and ketone trioses in glycerose results in the production of a ketose isomeric with lævulose, thus:



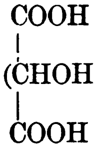
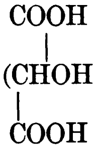
$$\underbrace{\underset{\text{(Glyceric aldehyde)}}{\begin{array}[b]{l}CH_3OH\\ |\\ CHOH\\ |\\ CHO\end{array}} + \underset{\text{(Dihydroxyacetone)}}{\begin{array}[t]{l}HCHOH\\ \;|\\ \;CO\\ \;|\\ \;CH_2OH\end{array}}}_{\text{(Glycerose)}} = \underset{\text{(Ketohexose)}}{\begin{array}{l}CH_2OH\\ |\\ CHOH\\ |\\ CHOH\\ |\\ CHOH\\ |\\ CO\\ |\\ CH_2OH\end{array}}$$

Such condensations are commonly called aldol condensations (see aldol, p. 104). By aldol condensation of six molecules of formaldehyde, formose is obtained, which contains an aldose identical with that obtained from glyceric aldehyde:



$$H_2CO + H\overset{\overset{H}{|}}{C}O + H\overset{\overset{H}{|}}{C}O + H\overset{\overset{H}{|}}{C}O + H\overset{\overset{H}{|}}{C}O + H\overset{\overset{H}{|}}{C}O =$$
$$= H_2COH\cdot CHOH\cdot CHOH\cdot CHOH\cdot CHOH\cdot CHO.$$

All the synthetic sugars are optically inactive when produced by purely chemical means.

Dextrose is the aldehyde of the hexacid alcohol *sorbitol*, $\begin{array}{l}CH_2OH\\ |\\ (CHOH)_4\\ |\\ CH_2OH\end{array}$, and can be converted into the latter by reduction. Dextrose can be oxidized to the dibasic acid *saccharic acid,*  $\begin{array}{l}COOH\\ |\\ (CHOH)_4.\\ |\\ COOH\end{array}$ The alcohol *dulcitol,* a stereoisomer of sorbitol, can be oxidized to galactose, and this aldehyde monosaccharide can be oxidized further to *mucic acid,*  $\begin{array}{l}COOH\\ |\\ (CHOH)_4.\\ |\\ COOH\end{array}$ Mucic acid is optically inactive, while saccharic acid is optically active.[1]

The question of the possibility of the formation of dextrose from proteid is of very great physiological importance. The chemistry of the problem will now be briefly considered. Attention has been called to the fact that proteids readily split up into amino-acids. Reasoning on purely chemical grounds it is possible that amino-acids containing three or six carbon atoms can be converted into dextrose.

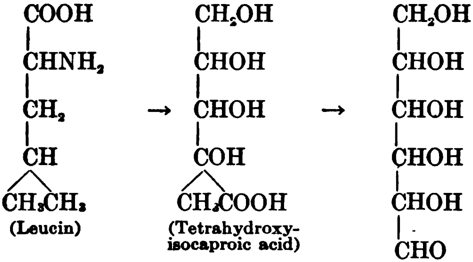
Alanin can be changed to lactic acid, the latter to glyceric acid, which can be reduced to glyceric aldehyde, and finally this can be converted into a dextrose-like sugar by aldol condensation. Such a synthesis when carried out in the animal organism would undoubtedly result in production of dextrose, i.e., dextrorotatory glucose. It is quite likely that serin (and possibly cystein) is also convertible into lactic acid and therefore into dextrose:

$$\begin{array}{lll}CH_2OH\cdot & CHNH_2 & \cdot COOH,\text{ serin.}\\ CH_3 & \cdot CHNH_2 & \cdot COOH,\text{ alanin.}\\ & \downarrow & \\ CH_3 & \cdot CHOH & \cdot COOH,\text{ lactic acid.}\\ & \downarrow & \\ CH_2OH\cdot & CHOH & \cdot COOH,\text{ glyceric acid.}\\ & \downarrow & \\ CH_2OH\cdot & CHOH & \cdot CHO,\text{ glyceric aldehyde.}\\ & \downarrow & \\ CH_2OH\cdot & (CHOH)_4 & \cdot CHO,\text{ dextrose-like aldose.}\end{array}$$

---

[1] There are eleven stereoisomeric acids having the formula $COOH(CHOH)_4COOH$.

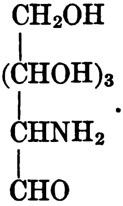
Leucin may be convertible into dextrose, since tetrahydroxycaproic acid can be made by the action of KOH on dextrose. A comparison of formulæ makes plain this possibility:



(Leucin) (Tetrahydroxy-isocaproic acid) (Dextrose)

The production of dextrose from alanin in the animal body has been experimentally demonstrated, lactic acid being noted as an intermediate product. In the case of leucin the experimental evidence is, at present, conflicting.

There are certain proteids that contain sugar combined with the proteid molecule proper;[1] such are called **glucoproteids.** This combined sugar has been found in most cases to be an aminohexose, generally *glucosamine*,



$$\begin{array}{l} CH_2OH \\ | \\ (CHOH)_3 \\ | \\ CHNH_2 \\ | \\ CHO \end{array}$$

. This sugar group in proteid may be

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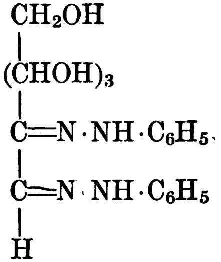
[1] In fact, most proteids except gelatin and casein contain such groups. In serum albumin, however, only a doubtful trace of such groups is present.

detected by certain colour reactions (see exp. below).

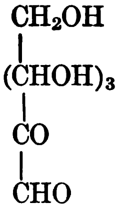
Experiment. To 1 c.c. of a strong solution of egg proteid add a drop of saturated solution of α-naphthol in alcohol (acetone-free); then with a pipette add 1 c.c. of C.P. H_2SO_4, so that the acid does not mix, but forms a bottom layer. The greenish colour at the zone of contact is due to the reagents; let the tube stand until a violet ring forms. If the violet colour does not appear, tap the tube so as to cause a slight mixing of the two layers. This is *Molisch's test* and is given by all carbohydrate-containing substances.

General Reactions of Monosaccharides. They all reduce alkaline silver, copper, and bismuth solutions, as do other aldehydes and some ketones (see p. 106). All form osazone crystals when treated with phenylhydrazine acetate (see exp. below). The osazone from lævulose is identical chemically with that from dextrose.

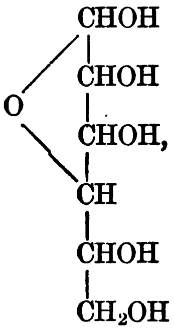
Methylphenylhydrazine gives osazones only with ketoses, and can therefore be used to detect the presence of lævulose. Glucosazone has the formula



$$\begin{array}{l} CH_2OH \\ | \\ (CHOH)_3 \\ | \\ C{=}N\cdot NH\cdot C_6H_5 \\ | \\ C{=}N\cdot NH\cdot C_6H_5 \\ | \\ H \end{array}$$

This can be converted by treatment with warm hydrochloric acid into glucosone,  $\begin{array}{c} CH_2OH \\ | \\ (CHOH)_3 \\ | \\ CO \\ | \\ CHO \end{array}$ When glucosone is treated with nascent hydrogen (as by using zinc dust), fructose is formed. Thus we can convert an aldose into a ketose.

Dextrose and galactose are dextrorotatory; lævulose is lævorotatory. They all have a different rotary power when freshly dissolved from that which they show after allowing the solution to stand. This phenomenon is called *multirotation*, and has been explained by supposing that in fresh solution the sugar molecules are oxides, as



but as the solution becomes older that these are changed to aldehyde (or ketone) molecules. These hexoses are fermented by yeast, giving, as the main products, alcohol and carbon dioxide.

In making a test for reducing sugar (dextrose, lævulose, or lactose) in the urine, reduction of Fehling's solution is not sufficient, for the urine may reduce this reagent after the administration of turpentine, chloroform, chloral, phenacetin, saccharin, salicylic acid and balsams, because these bodies are excreted in glycuronic acid combination (see p. 172). While the bismuth test excludes many non-saccharine substances that reduce Fehling's solution, it may yet be positive with urine after the administration of antipyrin, salol, turpentine, kairin, senna, rhubarb, and some other drugs. The phenylhydrazine test is the most delicate and the most positive. The fermentation test, if positive, is conclusive evidence. If lactose or a pentose alone be present, fermentation will not occur.

Dextrose (glucose, grape sugar) is present in many fruits and plants, in honey, and in the urine of diabetic patients. Commercial glucose is made by boiling starch with dilute acid; it is used for making candies, cheap syrup, etc. Pure glucose is crystalline; if crystallized from water it contains a molecule of water of crystallization, but if crystallized from methyl alcohol it is anhydrous. It is not so sweet as cane sugar.

Galactose is obtained from lactose by hydrolysis of the latter.

Lævulose (fructose, fruit sugar) is contained in many sweet fruits, in honey, and rarely in urine. It is difficult to crystallize.

EXPERIMENTS. (1) Prepare *osazone* crystals from dextrose and lævulose as follows: To 100 c.c. of a strong solution of the sugar add 0.25 gm. of phenylhydrazine hydrochloride and 0.5 gm. of sodium acetate, heat in a water bath at 100° for an hour, and cool. Examine the yellow crystals under the microscope. Collect the crystals on a filter, wash thoroughly with water acidulated with acetic acid, press between filter-paper, dry the crystals in a desiccator, and later make melting-point determinations.[1]

The osazones of the important sugars have the following melting-points:

Dextrose Lævulose	204°–205°
Lactose	200°
Maltose	206°

(2) *Ketose test.* To a few cubic centimetres of lævulose solution add half its volume of HCl. Add a few crystals of resorcin and heat the mixture. A deep-red colour develops, later a brown precipitate which is soluble in alcohol. The alcoholic solution is red.

(3) (*a*) Try the aldehyde tests (see p. 106) with dextrose solution. (*b*) To some dextrose solution add one fifth its volume of alkaline bismuth reagent (4 gm. Rochelle salts and 2 gm. of bismuth subnitrate dissolved in 100 c.c. of 10% NaOH), boil five minutes. On cooling a black precipitate separates out.

DISACCHARIDES.

These are the result theoretically of the union of two monosaccharide molecules, with the elimination of a molecule of water, çane sugar being a combination of dextrose and lævulose, lactose of dextrose and galactose, and maltose of two dextrose molecules:

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[1] A quicker and more satisfactory way of securing osazone crystals is as follows: To 0.5 c.c. phenylhydrazine add 0.5 c.c. glacial acetic acid, after mixing add 10 c.c. of the sugar solution, heat in a boiling water bath; glucosazone crystals appear in 5–10 minutes. For lact- and maltosazone heat 20–30 minutes, then cool before examining.

$$C_6H_{12}O_6 + C_6H_{12}O_6 = C_{12}H_{22}O_{11} + H_2O.$$

By hydrolysis the constituent monosaccharides are easily obtained:

$$C_{12}H_{22}O_{11} + H_2O = C_6H_{12}O_6 + C_6H_{12}O_6.$$

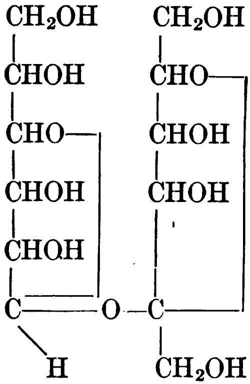
Dilute mineral acids and ferments (invertases) bring about this hydrolysis, which is called *inversion.* Yeast produces an invertase that hydrolyzes maltose quickly and cane sugar slowly, but has no effect on lactose. Therefore lactose does not ferment with yeast, while cane sugar and maltose do.

Maltose and lactose reduce alkaline copper and bismuth solutions, pure cane sugar does not. After inversion, however, cane sugar reduces these reagents. Therefore Fehling's solution can be used for quantitative estimation of all the sugars treated of in this chapter. 10 c.c. of Fehling's solution is reduced by

0.050	gram	dextrose or lævulose.
0.0676	"	lactose.
0.074	"	maltose.
0.0475	"	cane sugar (after conversion into invert-sugar).

Maltose and lactose form osazones with phenylhydrazine, each of these having a characteristic crystalline form and melting-point (see p. 219), while cane sugar forms no such combination provided hydrolysis is guarded against.

In order to explain the non-aldehydic action of cane sugar as shown by its behaviour in these two reactions the following formula has been suggested for it:



(Dextrose half) (Lævulose half)

These disaccharides are all dextrorotatory. Maltose shows the greatest rotary power, lactose the least; maltose and lactose manifest multirotation. Invert-sugar is distinctly lævorotatory, while the cane sugar from which it is produced is dextrorotatory; this is due to the fact that the lævulose produced (invert-sugar is a mixture of equal parts of lævulose and dextrose) rotates polarized light more to the left than does dextrose to the right.

Saccharose (cane sugar, beet sugar, sucrose), $C_{12}H_{22}O_{11}$, is the most important of the sugars because of its use as food. It is contained in sugar cane, beets, the sap of certain maple trees, and in many other vegetables and plants.

The method of commercial preparation of cane sugar is, in brief, as follows: The crushed or chipped material is soaked with water; this sugar extract is treated with lime (removes acids and many impurities), then with carbon dioxide (removes the lime), and is then evaporated in vacuum pans. On cooling, sugar crystallizes out. This crude sugar is dissolved, filtered through bone-black (animal charcoal), and recrystallized. The syrup that is left is *molasses*. Cane sugar as sold is commonly called granulated sugar.

Cane sugar forms large crystals when slowly crystallized; they are monoclinic prisms. It melts at 160°; at 210°–220° it is converted into caramel with loss of water. It is extremely soluble. It forms saccharates with bases.

Lactose (milk sugar), $C_{12}H_{22}O_{11} + H_2O$, is the sugar contained in milk. It occasionally occurs in the urine of pregnant women. Certain microörganisms convert lactose into lactic acid (souring of milk, see p. 169). When heated it forms lactocaramel, $C_6H_{10}O_5$. Lactose is crystalline and contains a molecule of water of crystallization. It can be obtained as amorphous lactose, which is anhydrous. Lactose forms compounds with bases. It is hydrolyzed by dilute mineral acids to galactose and dextrose.

Maltose, $C_{12}H_{22}O_{11} + H_2O$, is the product of the action of the ferments diastase (in malt), ptyalin (in saliva), or amylopsin (in pancreatic juice) upon starch. It can also be obtained from starch by treatment with dilute mineral acids, the action of the acid being stopped at a stage before glucose is formed. It crystallizes in fine needles. It can be easily hydrolyzed to dextrose.

EXPERIMENTS. (1) Produce osazone crystals from lactose and from maltose (see p. 218). Examine microscopically. Make melting-point determinations.

(2) (*a*) Examine a 10% solution of pure cane sugar with the polariscope (see p. 178). (*b*) To 50 c.c. of a 20% cane sugar solution in a 100 c.c. graduated flask add 1 gm. of citric acid, and boil for five minutes. Cool, almost neutralize, and fill up to the mark. Examine this invert-sugar solution (corresponding in concentration to the solution in (*a*)) with the polariscope. The specific rotation $[\alpha]D$ of the important sugars in 10% solution when sodium light is used are for

Dextrose	+ 52.7°
Lævulose	− 93.0°
Maltose	+137.04°
Lactose	+ 52.5°
Cane sugar	+ 66.54°
Invert-sugar	− 20.2°

(−means rotation to the left.)

(3) Test cane sugar before and after inversion (solutions of experiment 2, *a* and *b*) with Fehling's solution.

(4) Try the ketose test (see p. 219) on cane sugar solution.

(5) *Galactose test.* To 10 c.c. of a strong solution of lactose add 3 c.c. of HNO_3 and boil for a few minutes. Now evaporate on a water bath to about 3 c.c. while stirring. Add 2 c.c. of water and cool. If no crystals of mucic acid separate out, let the material stand and examine after twenty-four hours.

POLYSACCHARIDES.

These have complex molecules containing many sugar molecules linked together.

Cellulose,[1] $(C_6H_{10}O_5)x$, is essential to all plants, being the chemical basis of the woody fibre. Cotton-fibre, hemp, flax, and the best filter-paper are almost entirely cellulose. Ordinary paper is composed mainly of cellulose. Cellulose is affected by only a few chemical agents; concentrated acids and alkalies and an ammoniacal solution of copper oxide (Schweitzer's reagent) are able to dissolve it. If unsized paper be treated momentarily with sulphuric acid, its surfaces become changed to *amyloid*, which renders the paper tough. Parchment paper is made in this way. If a solution of cellulose in sulphuric acid be diluted and boiled, dextrin and glucose are produced by hydrolysis of the cellulose.

EXPERIMENTS. (1) Dissolve some scraps of filter-paper in a little cold concentrated H_2SO_4, dilute with 200 c.c. of water, and boil for an hour. Neutralize some of this hydrolyzed cellulose solution and test with Fehling's solution.

(2) Immerse a piece of blotting-paper in 80% H_2SO_4 for a moment only, transfer to a large beaker of water, and wash out the acid thoroughly. Allow the paper to dry out; it will be found to be tough.

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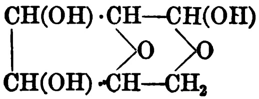
[1] The following formula has recently been proposed for cellulose:



(3) Detection of lignin[1] in paper made from wood. Coat a sheet of cheap white paper with a solution of aniline in HCl; if it turns yellow, lignin is present.

When cellulose is treated with nitric acid, **nitrates of cellulose** are formed, just as nitroglycerol is produced from glycerol. The nitrates range from the dinitrate to the hexanitrate.

Guncotton (nitrocellulose, pyroxylin) contains the higher nitrates. It is explosive. The hexanitrate is the basis of one of the best smokeless powders. The products of the explosion are nitrogen, hydrogen, carbon monoxide and dioxide, and water-vapour.

The lower nitrates are contained in *celloidin*. *Collodion* is a solution of these nitrates in a mixture of ether and alcohol. *Celluloid* is made by dissolving them in camphor.

An artificial silk can be produced by means of the hexanitrate, fine filaments being made and spun into thread. After being woven the nitrocellulose fabric is treated with a solution of calcium sulphide, which removes the NO_2 groups. Almost pure cellulose, resembling silk, is left.

EXPERIMENT. Mix 5 c.c. of C.P. HNO_3 and 10 c.c. of C.P. H_2SO_4. When cool immerse some absorbent cotton in the mixture for half a minute, then wash out the acid from the cotton with a large quantity of water, press out the water, and dry at room temperature. When dry, shake part of it with a mixture of ether and alcohol, pour the liquid into an evaporating dish and allow to evaporate. A syrupy liquid (collodion) is obtained, and later a glassy skin. Test the inflammability of another piece of the dry cotton, and compare with untreated cotton.

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[1] A substance (probably not a polysaccharide) present along with cellulose in wood.

Starch (amylum), $(C_6H_{10}O_5)x$, comprises a large part of all vegetable food. It exists in the plant as granules, having different forms and sizes in different plants. The granule has a membrane of cellulose enveloping it. This bursts when starch is heated with water, because the starch swells.

Starch is insoluble in cold water. When boiled, it apparently goes into solution or forms a gelatinous mass, according to the amount of water present. It is not a true solution, however, but is called a colloidal solution. Colloids in solution will not dialyze, i.e., pass through an animal membrane, parchment paper, or a semipermeable membrane (see p. 41). They exert no appreciable osmotic pressure and do not seem to obey the laws of depression of freezing-point, etc.; therefore their molecular weights are still undetermined.

Ordinary starch is made from corn or potatoes. A dilute solution of boiled starch is readily hydrolyzed by ferments (diastase, ptyalin, etc.) and by platinum black (catalytic action) at a temperature of about 40°. Dextrin is first formed, then maltose, while hydrolysis by boiling with dilute mineral acid carries the process further, the end product being glucose. Heat alone converts starch into dextrin; the crust on bread is mainly dextrin. Starch combines with iodine to form a blue compound; heat drives the iodine out of combination, so that the colour is lost until the mixture becomes cool again.

Dextrin, or more properly dextrins, are less complex bodies than starch. The formula $C_{36}H_{62}O_{31}$ has been assigned to some of them. Commercial dextrin is prepared from starch by means of heat. It forms a gummy solution which is used for making labels. It is insoluble in alcohol. All the dextrins except achroödextrin are precipitated by saturating their solutions with salts, such as ammonium sulphate and sodium sulphate.

Most of the dextrins give a red or violet colour with iodine. The dextrins are dextrorotatory. Acid hydrolyzes them to glucose.

Glycogen, $(C_6H_{10}O_5)x$, resembles dextrin. It is found only in animal tissues, mainly in the liver. The liver acts as a storehouse for carbohydrates, storing up in the form of glycogen the sugar which comes to it from the digestive organs, and then reconverting the latter into sugar as needed by the tissues. Glycogen forms a colloidal solution which is characteristically opalescent. With iodine it gives a reddish-brown colour. It hydrolyzes to dextrose. It is precipitated by 50% alcohol and by basic lead acetate.

EXPERIMENTS. (1) Test solutions of starch, dextrin, and glycogen with iodine solution.

(2) Test them with lead subacetate solution.

(3) Test them with Fehling's solution before and after hydrolyzing by boiling with dilute HCl.

Gums contain polysaccharides similar to dextrin. *Gum arabic* (acacia) contains arabin ($C_{10}H_{18}O_9$?), which hydrolyzes to arabinose. *Gum tragacanth* contains bassorin.

GLUCOSIDES.

These are vegetable substances which can be split up by hydrolysis into a sugar and some other characteristic compound or compounds. Many of them are important medicines. More than a hundred glucosides have been studied. The sugar derived from them is generally glucose.

Phloridzin, $C_{21}H_{24}O_{10}$, is used to produce experimental diabetes in animals. It splits up into glucose and phloretin, $C_{15}H_{14}O_5$ (see also phloroglucin, p. 267).

Salicin, $C_{13}H_{18}O_7$, is used in medicine (see p. 297).

Saponin, $C_{32}H_{52}O_{17}$, is contained in soap-bark. It forms a suds with water similar to soap-suds.

Amygdalin, $C_{20}H_{27}NO_{11}$, is found in bitter almonds, peach-pits, etc. The ferment emulsin, as well as acids, hydrolyze it to glucose, hydrocyanic acid, and benzaldehyde (see p. 270).

Digitalein, $C_{22}H_{38}O_9$, is contained in the very important drug digitalis. Glucose and digitaliretin, $C_{16}H_{26}O_3$, are the products of its hydrolysis.

Adonidin and *ergotinic acid* are also glucosidal in nature.

EXPERIMENTS. (1) Try Molisch's test (see p. 216) on a solution of a glucoside (e.g., saponin).

(2) Hydrolyze some glucoside solution by boiling with dilute H_2SO_4, neutralize, and examine for sugar with Fehling's solution.

CHAPTER XXI.

UNSATURATED HYDROCARBONS AND THEIR DERIVATIVES.

THE most important unsaturated hydrocarbons are the *ethylenes* and *acetylenes*. Their unsaturation consists in having two or three bonds or linkings between two or more carbon atoms, thus:

$$C{=}C,\ C{\equiv}C,\ C{=}C{-}C{=}C,\ C{=}C{=}C,\ \text{etc.}$$

Unsaturated substances of this nature readily form addition compounds, as with iodine and bromine. This fact is taken advantage of in analysis of fats and oils, the estimation of the oleic and other unsaturated acids being made by the use of an iodine solution (see p. 151).

Another illustration of the formation of addition compounds is the production of ethylene bromide, $C_2H_4+Br_2=C_2H_4Br_2$. Halogen acids (HBr, HI) are added on to these hydrocarbons in similar manner: $C_2H_4+HBr=C_2H_5Br$. The addition compound is, of course, saturated.

ETHYLENES.

Ethylenes or olefins, C_nH_{2n}, form an homologous series.

Ethylene (ethene, olefiant gas), $CH_2{=}CH_2$, is the only member of importance, and is contained in coal-gas (about 4%). It is colourless and burns with a yellow flame. Ethylene forms an explosive mixture with oxygen. It is obtained by dehydration of alcohol, as by sulphuric acid (see exp. below): $C_2H_5OH = C_2H_4 + H_2O$.

EXPERIMENTS. (1) In a litre flask heat a mixture of 30 c.c. of alcohol and 83 c.c. of C.P. H_2SO_4 on a sand-bath. Put a little sand in the flask. Use a two-holed cork. Insert a dropping funnel. Connect with a series of wash-bottles as shown in the diagram; the first bottle contains H_2SO_4, the Woulff bottle (having a safety-tube) contains dilute NaOH solution, each of

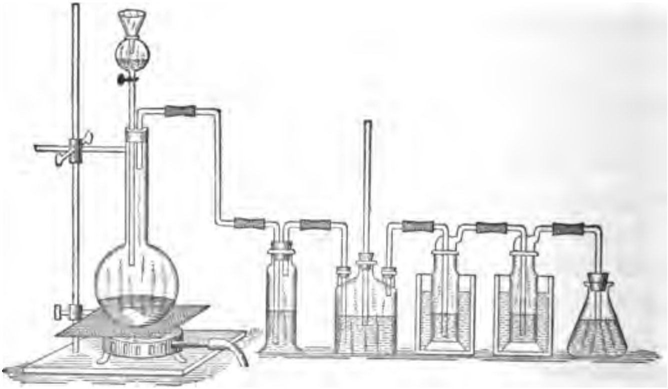

FIG. 24. .

the last bottles contains 10 c.c. of bromine and 25 c.c. of water, finally a flask containing dilute alkali catches any bromine vapour that may pass over. Begin heating the flask. At the start raise the safety-tube of the Woulff bottle out of the liquid, and attach a piece of tubing. By means of this tube bubble the evolved ethylene through a mixture of solutions of potassium permanganate and sodium carbonate in a test-tube (Von Baeyer's reagent[1]) until the pink colour is lost and a brownish precipitate of hydrated manganese dioxide appears. Lower the safety-tube and then begin running slowly into the flask, through the dropping funnel, a mixture of alcohol and sulphuric acid (100 c.c. of the former to 85 c.c. of the latter). Keep up a steady production of ethylene until the bromine is decolorized. The bromine bottles should stand in ice-water.

Disconnect the flask and then remove the flame. Wash the ethylene bromide repeatedly with water in a separating funnel, and finally shake it with NaOH solution. Draw off the bromide into a flask, add dry calcium chloride, and cork. After a day or so distil, noting the boiling-point (131°, but 129.5° at 730 mm.). Also take the specific gravity (2.1785 at 20°).

(2) Bubble coal-gas into Von Baeyer's reagent, as above.

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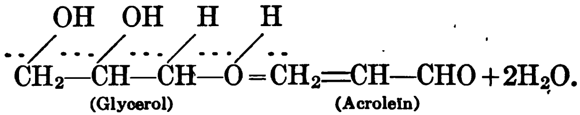
[1] Von Baeyer's reagent is decolorized by formic and hydroxybenzoic acids, by malonic ether, phenols, aldehyde, benzaldehyde, aldehyde bisulphite, acetone, acetophenone, glycerol, and some sugars (because of oxidation of these substances), as well as by unsaturated compounds.

Allyl alcohol (propenol), $CH_2{=}CH{\cdot}CH_2OH$, is an unsaturated alcohol corresponding to the hydrocarbon propene, $CH_2{=}CH{\cdot}CH_3$. Its radicle, C_3H_5, is called *allyl*. This alcohol can be made from glycerol.

Acroleïn (acrylic aldehyde), $CH_2{=}CH{\cdot}CHO$, is the aldehyde from the above alcohol. It is produced from glycerol (see p. 148):



$$\underset{\text{(Glycerol)}}{\overset{OH}{CH_2}{-}\overset{OH}{CH}{-}\overset{H}{CH}{-}\overset{H}{O}} = \underset{\text{(Acroleïn)}}{CH_2{=}CH{-}CHO} + 2H_2O.$$

By oxidation it becomes **acrylic acid,** $CH_2{=}CH{\cdot}COOH$.

Oleic acid is a member of the acrylic acid series. It has the formula $C_{18}H_{34}O_2$ or $C_{17}H_{33}{\cdot}COOH$. It is contained in combination with glycerol as glyceryl trioleate, in many oils, as in olive oil and whale oil, and in animal fats. Oleic acid forms crystals, melting at 14°. Hydriodic acid converts it into stearic acid; this is brought about by addition of hydrogen, thus:

$$\underset{\text{(Oleic acid)}}{C_{18}H_{34}O_2} + 2H = \underset{\text{(Stearic acid)}}{C_{18}H_{36}O_2}.$$

Fusion with caustic potash results in the formation of palmitic and acetic acids.

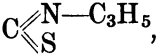
EXPERIMENTS. (1) Dissolve two drops of oleic acid in a few cubic centimetres of ether in a test-tube; shake with a little Von Baeyer's reagent (see p. 231).

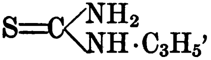
(2) Shake some ether with a little bromine water; the ether becomes yellow. Add a few drops of oleic acid and shake. The bromine is taken up, so that the colour is lost.

Ricinoleic acid is $C_{17}H_{32}(OH)COOH$. It is present in castor oil in combination with glycerol.

Crotonic acid, $CH_3\cdot CH{=}CH\cdot COOH$, is found in croton oil.

Allyl sulphide, $(C_3H_5)_2S$, is contained in oil of garlic. It has a disagreeable odour.

Allyl isothiocyanate,  $C\!\begin{array}{l} {=}N{-}C_3H_5 \\ {=}S \end{array}$, is a mustard oil. It is contained in glucosidal combination in mustard and horse-radish.

Allyl thiourea (allyl sulphocarbamide, thiosinamine),  $S{=}C\!\begin{array}{l} {-}NH_2 \\ {-}NH\cdot C_3H_5 \end{array}$, is used as a remedy.

ACETYLENES.

These hydrocarbons, C_nH_{2n-2}, form a series of which few members are known.

Acetylene, $CH{\equiv}CH$, is the only important member. Small quantities are synthesized directly from carbon and hydrogen when a stream of hydrogen is passed between the carbon poles of an electric arc-light, a small quantity of methane being formed at the same time. It is formed when a Bunsen burner "snaps back." The gas is made most easily and cheaply by the action of water on calcium carbide,

$$C_2Ca+2H_2O=C_2H_2+Ca(OH)_2.$$

When used with a special burner it gives a brilliant light. It is used extensively as an illuminating gas. It is a colourless gas of unpleasant odour.

EXPERIMENTS. (1) Put 10 gm. of calcium carbide in a dry flask or bottle, cork with a two-holed cork. By one hole suspend a dropping funnel containing water, into the other hole fit a bent delivery tube. Let the water drop on the carbide very slowly. Bubble the acetylene into Von Baeyer's reagent until the test is secured. Then connect with a platinum-tipped glass tube such as is used for burning hydrogen. Light the acetylene—a brilliant flame is obtained.

(2) Cause a Bunsen burner to strike back by blowing on the flame, invert over it a beaker which is moistened inside with a solution of cuprous chloride in ammonia—a red precipitate of copper acetylide is formed.

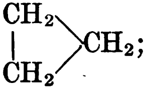
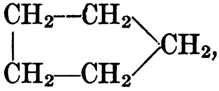
Linoleic acid, $C_{17}H_{31} \cdot COOH$, is contained in linseed oil in combination with glycerol. It has the power of taking up oxygen from the air, and then becomes a solid substance. Linseed oil in drying becomes hard for this reason, hence its use in varnishes and paints.

CHAPTER XXII.

CYCLIC COMPOUNDS AND TERPENES.

These form a transitional group between the fatty and the aromatic compounds.

CYCLIC COMPOUNDS.

Certain hydrocarbons with the general formula C_nH_{2n} have properties quite different from those of the ethylene series; indeed, they behave quite like members of the methane series. Thus, they do not reduce Von Baeyer's reagent. Therefore, instead of representing them as composed of an open chain with double linkings, their formulæ are written as closed chains (and hence they are called cyclic compounds); for example, cyclopropane, ; cyclopentane, , etc. They are given the same names as the members of the methane series, with the prefix cyclo. Certain of these cyclic compounds have been found in Caucasian petroleum.

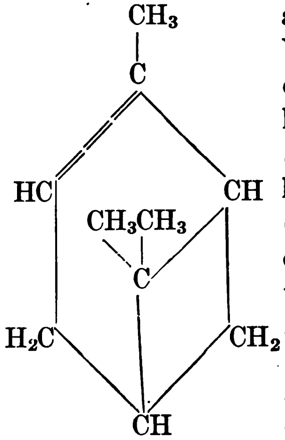
TERPENES AND CAMPHORS.

In the volatile oils obtained from coniferous trees (and in various other natural products) are contained bodies having the empirical formula $C_{10}H_{16}$. These are called terpenes. They decolorize Von

Baeyer's reagent (see p. 231), and they combine directly with one or two molecules of HCl. They therefore possess the general properties of unsaturated compounds, but yet they differ from these in many respects and may be considered to belong to the class of cyclic compounds since they contain a closed chain of carbon atoms. By mild oxidation many of them can be converted into cymene (paramethyisopropyl benzene) (see p. 253) and by further oxidation into paratoluic acid (see p. 278), both of these substances being aromatic compounds.

The terpenes and camphors include many bodies of medical and commercial value, and of these the following are important:

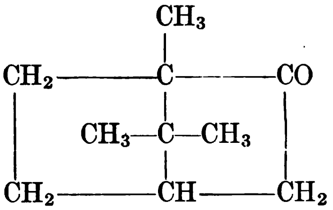
1. **Pinene,** $C_{10}H_{16}$, the principal constituent of oil of turpentine, has the structural formula annexed, and exists as stereoisomers. When combined with hydrochloric acid it forms pinene hydrochloride, $C_{10}H_{17}Cl$, which, since it resembles camphor, is known as *artificial camphor* (see exp. below). Artificial camphor can be converted into true camphor. *Oil of turpentine* is obtained by incising the bark of fir-trees; the crude oil contains, in addition to turpentine, residues constituting rosin. Pinene can be converted by alcohol and nitric acid into **terpin hydrate,** $C_{10}H_{18}(OH)_2+H_2O$, which is a crystalline substance used in medicine,

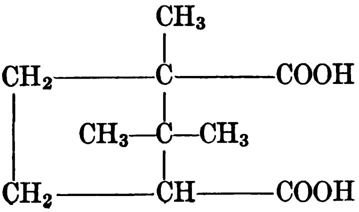


Experiments. (1) Prepare artificial camphor. Into 10 c.c. of freshly distilled turpentine that is free of water (treat with calcium chloride before distilling) contained in a flask kept cool by a freezing-mixture, bubble dry HCl gas until crystals of pinene hydrochloride appear. Make the HCl by heating in a retort a mixture of dried NaCl and C.P. H_2SO_4. Collect the crystals on a filter and examine them.

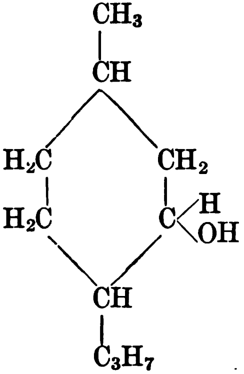
(2) Shake some turpentine with Von Baeyer's reagent. Is there evidence of unsaturated linking?

2. **Camphor,** $C_{10}H_{16}O$. This is a gum obtained by distilling with steam the finely chopped wood of the camphor tree. Its chemical structure has recently been worked out, and it can be produced by synthetic processes. Camphor contains a ketone group, having the formula as shown opposite. Carvacrol (isomeric with thymol) can be obtained from it by the loss of two atoms of hydrogen. By warming with phosphorus pentoxide it is converted into cymene. It melts at 176.4°, and sublimes, the sublimate forming crystals. *Camphor monobromide* is $C_{10}H_{15}BrO$. Camphor can be oxidized to *camphoric acid* (see formula opposite).





3. **Menthol** is related to camphor, but contains an alcohol group CHOH instead of a ketone group. Its formula is given below. Like camphor, it contains no unsaturated linkings. Menthol is a white crystalline substance melting at 42°, and is the chief constituent of oil of peppermint. It is useful as a medicine.



SUBSTANCES ALLIED TO TERPENES.

Caoutchouc or **rubber** contains a terpene-like substance, $C_{30}H_{68}O_{10}$. This is decomposable into $3(C_{10}H_{16})+10H_2O$. Rubber is the hardened milky juice of certain tropical plants. **Gutta-percha** is similar to rubber.

Cholesterol[1] (cholesterin), $C_{27}H_{44}O$ or $C_{27}H_{46}O$, is an important constituent of bile. Its chemical reactions

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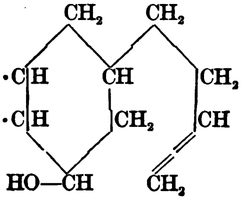
[1] The following structural formula has been proposed very recently:



reveal the presence of alcoholic hydroxyl and of double linkings between certain of its carbon atoms. It seems to be closely allied to the terpenes, and has no similarity in structure to fats, although in its solubilities it is much like them.

CHAPTER XXIII.

THE AROMATIC HYDROCARBONS.

NEARLY all of the substances which we have so far studied are represented in their formulæ as composed of open chains of carbon atoms. A few of them, such as the anhydrides of hydroxy-acids, lactones, and the purin derivatives, have to be represented as composed of closed chains. It is only in the case of the aromatic bodies and the cyclic compounds, however, that each link in the closed chain is represented by a C atom. In connection with the paraffin derivatives containing closed chains, moreover, it will be remembered that their closed chain is readily opened, e.g., an anhydride of an acid can easily be converted into the corresponding acid, etc.

We come now to a group of organic substances—the largest group, indeed—the members of which are composed of closed chains that cannot readily be opened. In the older chemical nomenclature the bodies belonging to this group were called aromatic bodies on account of the presence of an agreeable aroma, and by this name they are still known. They may all be looked upon as derivatives of a substance called benzene, C_6H_6, just as all the fatty substances may be represented as derivatives of methane. Many of the derivatives of benzene are indeed quite analogous with those of methane, undergoing similar reactions and possessing much the same properties. Unlike the fatty series, few of them are useful as foods; many of them, however, have very pronounced physiological actions. Commercially they are of very great value.

There are four simple reactions in which the two groups—i.e., the aromatic and the fatty—give very different results:

1. With concentrated nitric acid the aromatic hydrocarbons readily form nitro compounds, which on reduction with nascent hydrogen yield amino-derivatives. Paraffins are unaffected by HNO_3.

$$a.\quad \underset{\text{(Benzene)}}{C_6H_5}\boxed{H + HO}NO_2 = \underset{\text{(Nitrobenzene)}}{C_6H_5NO_2} + H_2O.$$

$$b.\quad C_6H_5NO_2 + 6H = \underset{\text{(Aniline)}}{C_6H_5NH_2} + 2H_2O.$$

2. With concentrated sulphuric acid they form sulphonic acids (see p. 163). Paraffins are unaffected by H_2SO_4.

$$C_6H_5\boxed{H + HO}\cdot SO_3H = \underset{\text{(Benzene sulphonic acid)}}{C_6H_5SO_3H} + H_2O.$$

3. Chlor- and brombenzene are very stable and do not readily react with KOH, whereas in the case of methyl chloride, etc., hydroxyl can readily be substituted for the Cl (see p. 93).

4. When a benzene substitution product with one or more side chains of carbon atoms is oxidized, the side chain or chains become oxidized in such a way as to form simply carboxyl.

BENZENE.

At the outset we must study the structure of benzene, since, as has been noted, this is the mother substance of the aromatic bodies. We must furnish evidence that its formula is correctly represented as having a closed chain.

Benzene[1] (benzol), C_6H_6. When coal is heated in gas retorts, in the preparation of artificial gas, there passes out with the gas a vapour which is condensed in specially arranged condensers. The condensed vapours constitute coal-tar. The ammonia and pyridine bases which are also given off from the retorts are dissolved in water. The tar is a mixture of neutral, acid, and a small quantity of basic bodies, and also contains particles of carbon in suspension (hence its blackness). The tar products are separated, partly by fractional distillation and partly by chemical means. The crude tar is distilled into four fractions, as follows:

(1) Light oil (fraction up to 170°).
(2) Carbolic oil (170°–230°).
(3) Heavy or creosote oil (230°–270°).
(4) Anthracene oil (above 270°).

The residue contains a large amount of carbon.

The light oil is purified by treatment with acid and with alkali and is then distilled. It is in the light oil that most of the benzene and its homologues are contained. The benzene can be further purified by fractional distillation, then by treatment with concentrated H_2SO_4 to remove thiophene (C_4H_4S), and finally by freezing it and pouring off the liquid portion.

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[1] Different from benzine (see p. 79).

Benzene may also be obtained (1) by distillation of a salt of an aromatic acid with soda-lime, a reduction which, it will be remembered, is analogous with that employed for the preparation of methane:

$$C_6H_5COONa + NaOH = Na_2CO_3 + C_6H_6.$$

(2) By passing acetylene (C_2H_2) through a red-hot tube. This method illustrates how synthesis of aromatic out of fatty hydrocarbons can be accomplished.

(3) By heating potassium in a current of CO. A synthesis occurs resulting in the formation of $C_6(OK)_6$, potassium carbonyl. This is a derivative of benzene and can be converted into benzene by distillation with zinc dust in the presence of water.

Benzene is a colourless liquid of aromatic odour, boiling at 80.3° (corrected) (at 79° at 742 mm.). Its melting-point is 4.96°. Its specific gravity is 0.8736 at $\frac{20°}{4°}$. Benzene is inflammable and immiscible with water. It can be used for molecular weight determinations (see p. 46).

Experiments. (1) Fractionally distil some light oil (see p. 13). At the first distilling collect as the first fraction all that comes over below 100°, for the second fraction that distilling between 100° and 115°, and for the third the balance of the distillate up to 140°. Treat the first fraction (containing water, ammonia, and thiophene as impurities) as follows: Filter it into a dry separating funnel; shake successively with several portions of

10 c.c. each of C.P. H_2SO_4 until the acid no longer becomes strongly coloured. Put the oily liquid into a flask and shake with finely broken solid NaOH. Filter into a fractionating flask or a flask to which is then attached a Hempel's column (see diagram, p. 14); redistil carefully, keeping the temperature below 82° as long as any distillate comes over. Notice the benzene odour of this distillate. Continue the fractional distillation with the other distillates in the usual manner, collecting fractions for each 10°. If time permits, refractionate these, and try to determine by odour the presence of toluene and xylene.

(2) Mix thoroughly 25 gm. of benzoic acid and 50 gm. of powdered quicklime, and put into a dry retort. Connect with a condenser and heat gradually. Treat the distillate with dry calcium chloride and redistil from a small fractionating flask (an air-condenser will do). Note the boiling-point. Put the distillate into a dry test-tube and cool in a freezing-mixture until crystallization occurs. Remove from the mixture and warm the test-tube with the fingers while stirring the crystals with a thermometer. At what point does the temperature remain while the crystals are melting?

(3) Determine the specific gravity of some pure benzene at 15° with the Westphal balance.

(4) Shake a few cubic centimetres of benzene with Von Baeyer's reagent. Does it act like an unsaturated compound?

Structure of Benzene. From its empirical formula, C_6H_6, one would expect to find benzene giving reactions like those of acetylene or other unsaturated hydrocarbons,[1] that is to say, reactions indicating the existence of double bonds between the carbon atoms. Such, however, is not the case. Benzene does not readily combine with halogens, i.e., form addition products; it is not sensitive toward oxidizing agents; it does not decolorize a solution of potassium permanganate containing sodium carbonate. Unsaturated compounds readily give all these reactions. It is evident, therefore, that the formula for benzene cannot be represented as containing double bonds between the carbon atoms. Further, the formula must represent all the hydrogen atoms as similarly combined with the carbon atoms, *for there are no isomers of the monosubstitution products of benzene:* there is only one monobrombenzene, one monochlorbenzene, etc. This important fact can be shown in a variety of ways. Perhaps the simplest is as follows: If we treat benzene with bromine one of the six halogen atoms is replaced by bromine. Numbering the hydrogen atoms thus: $\overset{1}{H}\,\overset{2}{H}\,\overset{3}{H}\,\overset{4}{H}\,\overset{5}{H}\,\overset{6}{H}$, let us suppose that $\overset{1}{H}$ is replaced. Our problem is to see whether the monobrombenzene thus formed is identical with that formed by replacement of $\overset{2}{H}$, $\overset{3}{H}$, etc. To do this we must replace another H in the compound $C_6\,\overset{1}{Br}\,\overset{2}{H}\,\overset{3}{H}\,\overset{4}{H}\,\overset{5}{H}\,\overset{6}{H}$ by some group which can then be substituted by Br, the Br originally present being meanwhile replaced by H. This can be accomplished by treating monobrombenzene with nitric acid, the resulting compound having the formula $C_6H_4BrNO_2$. For the sake of argument, let us suppose that $\overset{2}{H}$ is replaced by the NO_2 group, thus: $C_6\,\overset{1}{Br}\,\overset{2}{NO_2}\,\overset{3}{H}\,\overset{4}{H}\,\overset{5}{H}\,\overset{6}{H}$. By the action of nascent H the NO_2 group becomes an amido group, NH_2 (see p. 283), and the Br is replaced by H. The formula for our substance is then $C_6\,\overset{1}{H}\,(\overset{2}{NH_2})\,\overset{3}{H}\,\overset{4}{H}\,\overset{5}{H}\,\overset{6}{H}$. By treating this with nitrous acid the diazonium salt is formed, which by treatment with hydrobromic acid (see p. 289) yields a monobrombenzene in which the Br atom stands in place of $\overset{2}{H}$, and yet this is found to be identical in properties with that monobrombenzene in which Br was in place of $\overset{1}{H}$. By similar reactions the various H atoms may be replaced one by one, the resulting monosubstitution product being always the same.

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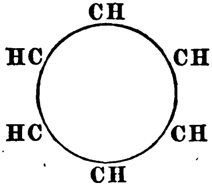
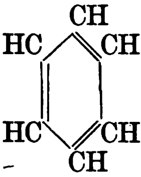
[1] Cf. dipropargyl, C_6H_6, $CH\equiv C-CH_2-CH_2-C\equiv CH$.

This fact makes it evident that we cannot represent the C atoms as linked together in an open chain, for then there would necessarily be two or three varieties of monosubstitution products, depending upon the particular C atom in the chain to which the substituting group is linked (*cf.* alcohols, p. 68). On this account Kekulé, who had been a mechanical engineer before he became a chemist, conceived the notion that the C atoms must be represented as forming a ring, and that the formula for benzene must be



or, as it is more usually written,

 .

To satisfy the quadrivalence of the C atom, it is necessary, as shown in the second formula, to assume that certain of these bonds are double. We have, however, seen that when double bonds between carbon atoms exist, the resulting body is unsaturated. To explain this apparent inconsistency, Kekulé supposes that in benzene there are really no double bonds in the same sense as they exist in unsaturated hydrocarbons, but that the double bond is *dynamic*, changing about from place to place, and is really unrepresentable in a formula.[1]

In perfect harmony with this conception of a ring is the fact that there are *three kinds of disubstitution products*. That three and only three are possible will be evident from the following formulæ, where x represents some substituting group:

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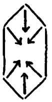
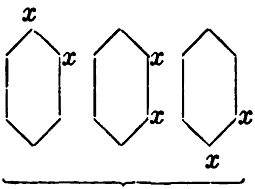
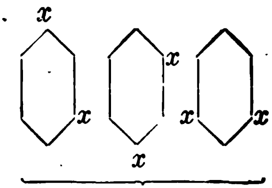
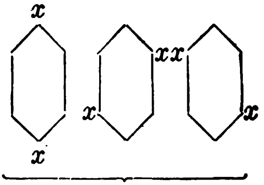
[1] The centric formula  has been proposed to indicate pictorially this self-saturation of the carbon atoms of the ring without definite extra linkings. This formula also has the advantage of emphasizing the distinguishing difference of all aromatic from other organic compounds.



A (ortho)



B (meta)



C (para)

The substituting groups may replace neighbouring hydrogens, as in the formulæ marked A; or be so arranged that a carbon of the ring intervenes, as in B; or with two such atoms intervening, as in C. Bodies exhibiting the first arrangement are called *ortho*, the second *meta*, and the third *para*.[1] For certain of the simple disubstitution products of benzene it has been definitely established which is ortho, which meta, and which para. To ascertain to which of these groups an unknown substance belongs it is necessary to transform it into one of the known simpler forms, it being considered that the unknown substance contains the same arrangement of its side chains as does the simpler substance which it yields. It remains for us to see, therefore, how it is possible to tell to what class some simple disubstitution product of benzene belongs. This is done by a study of the number of isomeric compounds which can be produced by substituting still another hydrogen atom of the ring. Suppose *y* represent this third substituting group. In an *ortho* compound we might have *y* attached next to *x*,

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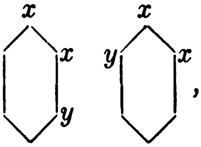
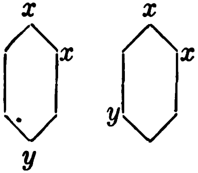
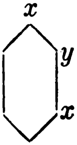
[1] The abbreviations *o*, *m*, and *p* are used for these terms.



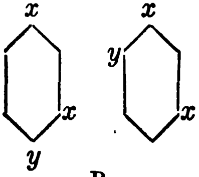
, or one carbon atom removed from it,



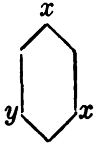
; that is to say, there might be two trisubstitution products which on removal of *y* would yield the same disubstitution product. In a *meta* compound *y* might occupy three positions which would be different; thus, between the two *x*'s as in A, or beyond but next to them as in B, or separated from them by carbon atoms of the ring as in C, thus:



A

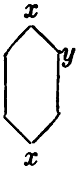


B

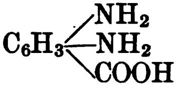


C

That is to say, there are three trisubstitution products which yield the same disubstitution product. In a *para* compound *y* could occupy only one position, i.e., next to an *x*; therefore there is only one trisubstitution product that could be converted into it, thus:



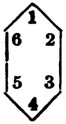
. To take an example: There are six diaminobenzoic acids with the formula



$$C_6H_3\begin{cases}NH_2\\NH_2\\COOH\end{cases}.$$

By removal of the carboxyl group three of these yield diaminobenzenes which are identical in properties (melting-point 63°), and which must therefore be meta; two others yield another variety of diaminobenzene (melting-point 102°) which must be ortho; and the remaining one yields yet another diaminobenzene (melting-point 140°) and which is para.

For convenience of description it is customary to number the carbon atoms in the benzene ring thus:



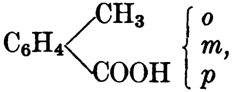
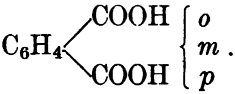
HOMOLOGUES OF BENZENE.

The chief homologues of benzene are toluene, $C_6H_5\cdot CH_3$, the xylenes, $C_6H_4(CH_3)_2$, mesitylene, $C_6H_3(CH_3)_3$, and durene, $C_6H_2(CH_3)_4$.

Toluene (toluol), $C_6H_5\cdot CH_3$, boiling-point 111°, specific gravity 0.8656 at $\frac{20°}{4°}$, can be separated from light oil or can be prepared synthetically by treating a mixture of monobrombenzene and methyl iodide with sodium (*cf.* synthesis of paraffins, p. 76):

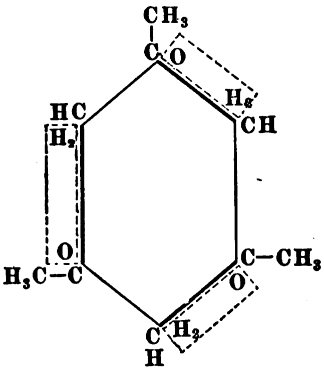
$$C_6H_5Br + CH_3I + 2Na = NaI + NaBr + C_6H_5CH_3.$$

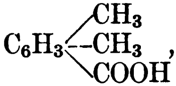
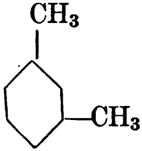
This reaction clearly illustrates its structure as methyl benzene. By oxidation the CH_3 group becomes carboxyl, *benzoic acid*, C_6H_5COOH, being therefore formed.

Xylenes, $C_6H_4(CH_3)_2$. Being disubstitution products of benzene, there are three of these. The boiling-point of ortho is 141.9°, meta 139.2°, para 138°; the specific gravity at $\frac{20°}{4°}$ of ortho is 0.8766, meta 0.8655, para 0.8635. The xylenes can be prepared from light oil. By oxidation they give first *toluic acids*,  $C_6H_4\left\langle\begin{matrix}CH_3\\COOH\end{matrix}\right.\left\{\begin{matrix}o\\m,\\p\end{matrix}\right.$ and then *phthalic acids*,  $C_6H_4\left\langle\begin{matrix}COOH\\COOH\end{matrix}\right.\left\{\begin{matrix}o\\m\\p\end{matrix}\right.$. The xylol, which is extensively used in histological work and as a fat-solvent, is a mixture of the xylenes.

Isomeric with the xylenes is **ethyl benzene,** $C_6H_5 \cdot C_2H_5$, which on oxidation yields benzoic acid, C_6H_5COOH, instead of toluic or phthalic acid.

Mesitylene, $C_6H_3(CH_3)_3$, boiling-point 164.5°, specific gravity 0.8694 at $\frac{9.8°}{4°}$, is also contained in light oil, and can likewise be obtained by a most interesting and important synthesis, viz., by distilling a mixture of acetone and sulphuric acid (see exp. below). Three acetone molecules no doubt enter into the synthesis, the sulphuric acid removing a molecule of water from each and causing them to condense together into a ring as represented in the following formula.



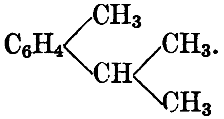
Mild oxidation of mesitylene yields *mesitylenic acid,*  $C_6H_3\begin{cases}CH_3\\CH_3\\COOH\end{cases}$, and if this be heated with soda-lime and the COOH group be thus removed (see p. 243), metaxylene is obtained, furnishing corroborative proof that metaxylene has the formula  .

EXPERIMENT. *Preparation of a benzene hydrocarbon (mesitylene) from a fatty compound (acetone).* Into a 500 c.c. flask put 100 gm. of clean sand, 50 c.c. of acetone, and a cooled mixture of 65 c.c. of C.P. H_2SO_4 and 30 c.c. of water. Mix thoroughly and allow to stand for at least two days. Distil, using an oil-bath. Shake the distillate with dilute alkali, then with water. Separate the oily layer, dry it with calcium chloride, and distil. Collect the fraction coming over above

150°. Notice the aromatic odour. Test it for *Friedel and Crafts' reaction* as follows· Place a few small crystals of anhydrous aluminium chloride in a dry test-tube; heat gradually until a thin coating of sublimate is secured in the upper part of the tube. When cool add a solution of a few drops of the mesitylene in about 2 c.c. of chloroform. Most aromatic hydrocarbons and some of their derivatives give a colour reaction under the conditions of this test.

Durene is of no importance.

Cymene is paramethylisopropyl benzene,



$$C_6H_4\Big\langle\begin{array}{l}CH_3\\ CH\Big\langle\begin{array}{l}CH_3.\\ CH_3\end{array}\end{array}$$

It can be obtained by warming camphor, $C_{10}H_{16}O$, with phosphorus pentoxide, or by treating pinene, $C_{10}H_{16}$ (from turpentine), with chlorine. It is a constituent of certain ethereal oils, as oil of *eucalyptus* and oil of *thyme*.

CHAPTER XXIV.

AROMATIC HALOGEN DERIVATIVES.[1]

Of Benzene. As already explained, there is only one kind of monohalogen substitution product of benzene. *Chlor- and brombenzene* can be prepared by treating benzene with chlorine or bromine. *Iodobenzene* is prepared with greater difficulty, it being necessary to have an oxidizing agent present (I_2 or Fe_2Cl_6). By prolonged action more than one hydrogen atom of the benzene molecule becomes replaced by the halogen, and of course there are *o*-, *m*-, and *p*-disubstitution products; indeed, all the H atoms may be replaced, hexachlor- (or brom-) benzene being formed, C_6Cl_6 (or C_6Br_6). If the reaction takes place in direct sunlight, addition products, instead of substitution products, are obtained, such as $C_6H_6Cl_6$ and $C_6H_6Br_6$. These readily decompose into the halogen acid and trisubstitution products of benzene:

$$C_6H_6Cl_6 = 3HCl + C_6H_3Cl_3.$$

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[1] It will be advisable for the student to look over the synopsis of aromatic compounds (p. 326) frequently in studying the following pages.

In contrast to the halogen derivatives of the paraffins, the halogen substitution products of benzene are very stable and do not readily give up their halogen atoms to be replaced by hydroxyl, a cyanide group, an amido group, etc., as alkyl halides do.

Of Toluene. There are four bodies with the empirical formula C_7H_7Cl. One of these, called *benzyl chloride*, has a very disagreeable odour and readily yields up its Cl atom when heated with hydroxides, cyanides, etc. It behaves in this respect like a fatty derivative. These facts suggest that the Cl atom is in the side chain, thus $C_6H_5CH_2Cl$. That this is really so is proven by the fact that when oxidized it yields benzoic acid, C_6H_5COOH. It is formed when toluene is treated at boiling temperature or in direct sunlight with the halogen.

The other three bodies are called *chlortoluenes* and have agreeable aromatic odours. They do not give up their Cl atom when heated with hydroxides, etc. They behave in this respect like chlorbenzene, so that the Cl atom must be present in direct connection with the benzene nucleus itself, thus: $C_6H_4\langle{}^{CH_3}_{Cl}$. The three varieties are ortho, meta, and para. When oxidized the Cl atom is not removed, but the CH_3 side chain becomes converted into COOH, a substituted benzoic acid being thus formed, i.e., a chlorbenzoic acid. They are prepared by treating toluene in the cold, and in diffused light, with chlorine, the reaction being greatly accelerated by the presence of antimony trichloride or some other halogen-carrier.

In the same way with the di- and trihalogen substitution products of toluene, substitution may occur either in the phenyl[1] or methyl groups. The other substitution products of toluene exhibit a similar isomerism.

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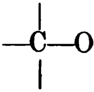
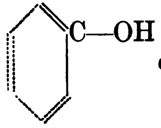
[1] Phenyl is the name given to the radicle C_6H_5.

CHAPTER XXV.

AROMATIC HYDROXY COMPOUNDS.

One or more of the H atoms of benzene may be displaced by a hydroxyl group —OH, the resulting body being called a phenol. In contrast to the feebly basic properties of the hydroxyl derivatives of the paraffins, viz., the alcohols, the phenols manifest faintly acid properties, so that some of them are called acids; thus, monohydroxybenzene is carbolic acid, and trihydroxybenzene, pyrogallic acid. Their acidity indicates that in solution a few $H^{\cdot}$ ions are liberated. When brought into contact with alkaline hydroxides, salts, called phenolates or phenoxides, are formed, e.g., C_6H_5ONa, sodium phenolate. Such phenolates can be obtained by dissolving the phenol in a solution of the hydroxide and evaporating to dryness. They are, therefore, stable in the presence of water and thus differ from the alcoholates, which are decomposed by water and can be formed only by acting on alcohol with the alkali metals. By union with phenyl, therefore, the hydroxyl group —OH comes to possess quite different properties than when it is combined with a paraffin (see p. 93).

On the other hand, even such weak acids as carbonic (H_2CO_3 or CO_2+H_2O) are more strongly acid than phenol and can decompose phenolates, liberating the phenol. The percentage dissociation for a decinormal solution of phenol is only 0.0037, that of carbonic acid being 0.174.

In other respects phenols behave like tertiary alcohols (*cf.* tertiary alcohol group  $-\overset{|}{\underset{|}{C}}-OH$ with  of phenol), thus: they form ethers and ethereal salts, but do not yield aldehydes, ketones, or acids on oxidation (see p. 71). The OH group can be removed by treatment with PCl_5. Using the same classification as for alcohols, we may, therefore, subdivide them into mon-, di-, and triacid phenols.

MONACID PHENOLS.

Phenol (carbolic acid), C_6H_5OH. This important substance is extracted from the carbolic oil fraction of coal-tar by shaking with a solution of alkali, the carbolic acid in the resulting solution being then precipitated by sulphuric acid and redistilled (see exp. below). It may also be prepared by fusing potassium benzene sulphonate with caustic potash:

$$\underset{\text{(Potassium benzene sulphonate)}}{C_6H_5SO_3K} + KOH = C_6H_5OH + K_2SO_3,$$

or by boiling a diazonium salt with water (see p. 238):

$$\underset{\text{(Benzene diazonium nitrate)}}{C_6H_5N_2 \cdot NO_3} + H_2O = C_6H_5OH + HNO_3 + N_2.$$

EXPERIMENTS. (1) Extract phenol from heavy oil (carbolic oil) in the following manner: Shake about

20 c.c. of the oil with an equal quantity of 10% NaOH solution. Filter the aqueous layer, acidulate the filtrate, cool, and shake with 10 c.c. of ether. Remove the ether with a pipette and evaporate in a porcelain dish on a steam bath or a hot water bath *away from a flame,* and preferably in a fume chamber. Test the residue for phenol (see tests below).

(2) *Prepare phenol from aniline.* Into a freshly made (hot) solution of 12 c.c. of C.P. H_2SO_4 in 50 c.c. of water put 10 c.c. of aniline, allowing it to flow down the wall of the beaker. Mix well and dilute with 100 c.c. of water. Cool with running water, then add sodium nitrite solution (8.5 gm. in 40 c.c. of water) until a drop of the mixture well diluted gives a blue colour to starch-potassium-iodide paper (soak filter-paper in boiled starch solution containing potassium iodide, dry it, and cut up into strips), showing the presence of free nitrous acid. This procedure is called *diazotizing,* because the nitrous acid changes the aniline salt into a diazonium salt. Transfer to a half-litre flask, heat to 40°–50° in a water bath for half an hour, then distil with steam (see p. 15). The phenol passes over into the condenser with the steam. Saturate the distillate with sodium chloride and shake with several small portions of ether. Dry the separated ethereal extract over dehydrated sodium sulphate for several days in a corked flask. Distil off the ether (away from a flame if possible, a steam-bath is safest); finally draw a stream of air through the hot flask with a suction-pump. Distil the phenol, using an air-condenser. Cool the distillate with ice-water; if crystals form, decant the liquid part and test it as below.

$$\underset{\text{(Aniline)}}{C_6H_5NH_2} + H_2SO_4 = \underset{\text{(Aniline sulphate)}}{C_6H_5NH_2 \cdot H_2SO_4},$$

$$C_6H_5 + NH_2 \cdot H_2SO_4HNO_2 = \underset{\text{(Benzene diazonium sulphate)}}{C_6H_5 \cdot N{=}N \cdot OSO_3H} + 2H_2O,$$

$$C_6H_5 \cdot N{=}N \cdot OSO_3H + H_2O = \underset{\text{(Phenol)}}{C_6H_5OH} + N_2 + H_2SO_4.$$

(3) *Tests.* (*a*) To half a test-tube of phenol solution add bromine water until a white precipitate of *tribromphenol* forms. (*b*) Test some solution with a drop of ferric chloride solution—a violet colour. (*c*) To a few cubic centimetres of solution add Millon's reagent and boil—a red colour or precipitate. (*d*) To 10 c.c. of phenol solution add a few cubic centimetres of ammonia, then small portions of bleaching-powder, shaking after each addition, until a blue colour is obtained.

Phenol, when pure, forms colourless rhombic needles melting at 39.6° and boiling at 182.9°. Its specific gravity is 1.039 at 58.5°. It becomes reddish on exposure to light. It dissolves in 20 parts of water at 17°; in other words, by shaking phenol crystals with water and allowing them to stand at room temperature an approximately 5% solution is obtained, and the crystals, by taking up water, will liquefy and form an oily layer at the bottom of the bottle. It mixes with alcohol and ether in all proportions. Phenol is extensively used in surgery as an antiseptic. It is produced in the intestine by the action of microörganisms on the aromatic groups in proteid; the phenol thus produced is absorbed into the blood and unites with potassium sulphate, to be excreted into the urine as potassium phenol sulphate. Phenol uncombined with alkali is poisonous. It is often taken with suicidal intent.

The **derivatives of phenol** are (1) the ethers and ethereal salts and (2) the substitution products.

The **ethers** are of two classes: (*a*) the *aromatic-fatty* ethers, such as *true aromatic* phenyl ethyl ether, $C_6H_5 \cdot O \cdot C_2H_5$, and (*b*) the ethers, such as phenyl ether, $C_6H_5 \cdot O \cdot C_6H_5$. The aromatic-fatty ethers may be obtained by allowing an alkyl halide to act on a phenolate:

$$C_6H_5O\boxed{Na + I}C_2H_5 = C_6H_5 \cdot O \cdot C_2H_5 + NaI.$$

The chief members of this class are *anisole* (phenyl methyl ether) and *phenetole* (phenyl ethyl ether). They are both liquids having pleasant odours. The true aromatic ethers cannot be prepared by this reaction, since a halogen cannot easily be displaced from phenyl. They may, however, be obtained by heating phenol witha dehydrating agent such as aluminium chloride:

$$C_6H_5O\boxed{H + HO}C_6H_5 = C_6H_5 \cdot O \cdot C_6H_5 + H_2O.$$

The **ethereal salts.** *Phenyl acetate,* $C_6H_5 \cdot OOCCH_3$, is a type of these and is prepared by the action of acetyl chloride on phenol:

$$C_6H_5O\boxed{H + Cl}OCCH_3 = C_6H_5 \cdot OOCCH_3 + HCl.$$

The **substitution products of phenol.** In these one or more hydrogens of phenyl (C_6H_5) are replaced by some radicle but the hydroxyl group remains intact. They form a large class, but only a few of the compounds will be discussed here, the most important of the others being considered later.

Tribromphenol, $C_6H_2Br_3OH$, is precipitated by treating phenol with bromine water (see exp. above).

Mononitrophenol, $C_6H_4(NO_2)OH$, may be ortho or para and is prepared by the action of dilute nitric acid on phenol.

Trinitrophenol, $C_6H_2(NO_2)_3OH$, or **picric acid,** is prepared by allowing strong nitric acid to act on phenol (see exp. below). It forms yellow prismatic crystals, has a bitter taste, and is very poisonous. In watery solution it stains silk and wool yellow and is used in histology for staining elastic fibres and also zymogen granules in gland cells. Like nitroglycerol, it is an explosive, and its potassium and ammonium salts are extensively employed for this purpose. The substitution of three H atoms by the negative NO_2 groups in picric acid evidently increases its acidity, i.e., its dissociability into $H^{\cdot}$ ions (kations) and anions of the rest of the molecule (see exp. below).

EXPERIMENTS. (1) *Prepare picric acid.* Put 10 gm. of C.P. HNO_3 into a flask, add slowly 10 gm. of phenol. When the action has subsided add 30 gm. of fuming nitric acid and boil until the liquid becomes yellow. Cool, dilute the crystalline mass with water, and filter with suction. Wash the crystals with water, and recrystallize from a considerable quantity of hot water which has been acidulated with 5 drops of H_2SO_4:

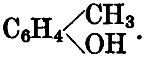
$$C_6H_5OH + 3HONO_2 = C_6H_2(NO_2)_3(OH) + 3H_2O.$$

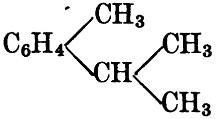
(2) Warm gently a little picric acid with 5 c.c. of petroleum ether in a test-tube; a colourless solution is secured (no ionization). Now add water and shake; the water becomes yellow from the picric acid dissolved in it (ionization).

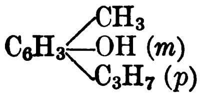
(3) Immerse pieces of woolen, silk, and cotton cloth in picric acid solution for fifteen minutes. Wash them thoroughly with running water. Which are dyed?

Aminophenols (see p. 296).

Phenolsulphonic acids (see p. 296).

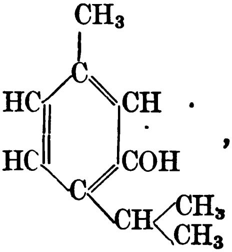
Cresols (hydroxytoluenes),  $C_6H_4\begin{matrix}\diagup CH_3\\ \diagdown OH\end{matrix}$. In accordance with the theory it is possible, by starting from the corresponding toluene-sulphonic acids or toluidines, to obtain three cresols, viz., ortho, meta, and para. They are contained, along with *guaiacol*, in **creosote,** a product of wood-tar, and sometimes used as an antiseptic. It is very difficult to separate the individual cresols from creosote. Cresol is also produced in the intestine by the action of microörganisms on proteid. **Creosotal** is the carbonate of creosote. **Lysol** is a mixture of cresols with soap, and is said to be as strongly germicidal but less irritating than phenol. **Creolin** forms with water an emulsion of cresols. These substances possess antiseptic properties and are less poisonous than phenol. They are extensively used for disinfecting purposes.

Thymol and **carvacrol** are isopropyl cresols. That this is so is shown by the fact that they can both be converted into cymene,  $C_6H_4\left\langle\begin{array}{l}CH_3\\ CH\left\langle\begin{array}{l}CH_3\\ CH_3\end{array}\right.\end{array}\right.$ (by removal of OH). They also give the reactions of phenols and might therefore be considered as hydroxycymenes. Thymol is isopropylmetacresol,



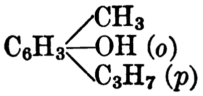
$C_6H_3\left\langle\begin{array}{l}CH_3\\ OH\ (m)\\ C_3H_7\ (p)\end{array}\right.$

or



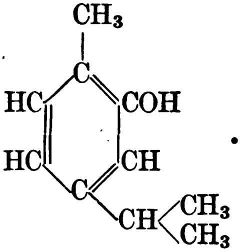
,

and carvacrol is isopropylorthocresol,



$C_6H_3\left\langle\begin{array}{l}CH_3\\ OH\ (o)\\ C_3H_7\ (p)\end{array}\right.$

or



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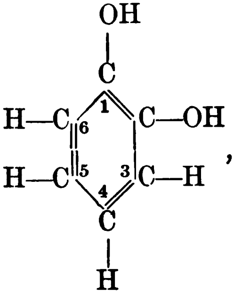
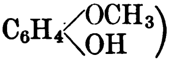
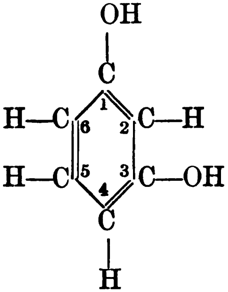
Thymol is contained in oil of thyme and is an antiseptic. It is crystalline and can be used for preserving urine. It is less poisonous than phenol. Melting-point 49.4° (corrected). Carvacrol is contained in *oil of caraway.*

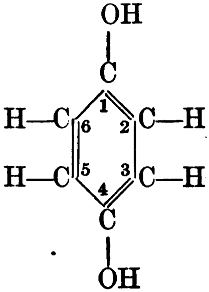
Aristol is dithymol di-iodide. It is an antiseptic powder.

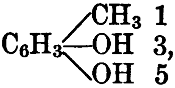
DIACID PHENOLS.

These are ortho, meta, and para. They all have more or less marked reducing properties, and on this account some of them (especially hydroquinol) are used as developers in photography. With ferric chloride they all give colour reactions by becoming partially oxidized.

Orthodihydroxybenzene, pyrocatechol (1, 2-phendiol, *pyrocatechin,* catechol),  , can be made by fusing orthophenol-sulphonic acid with caustic potash. It is soluble in water. By introducing a methyl radicle in place of a hydrogen atom of a hydroxyl group **guaiacol** (monomethyl ether of pyrocatechol,  $C_6H_4<\begin{matrix}OCH_3\\OH\end{matrix}$) is obtained. This latter can also be separated from beech-wood tar by distillation and crystallization, and is sometimes used, particularly as one of its compounds, in the treatment of phthisis. Guaiacol benzoate or **benzosol** and guaiacol carbonate, $(C_6H_4{\cdot}OCH_3\ O)_2CO$, have also been much used as remedies for tuberculosis.

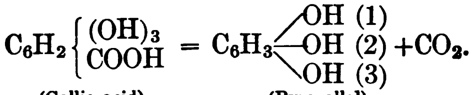
Metadihydroxybenzene, resorcinol (1, 3-phendiol, resorcin),  , is made by fusing metabenzene-disulphonic acid with caustic potash. Soluble in water, its solutions have a sweetish taste. When heated with phthalic acid it forms fluorescein (see exp., p. 280), and with sodium nitrite a blue pigment, *lacmoid*, solutions of which turn red with acids.

Paradihydroxybenzene, hydroquinol (hydroquinone quinol, 1. 4-phendiol),  , is extensively used in photography.

Dihydroxytoluene, orcinol (orcin),  $C_6H_3\begin{cases} CH_3 & 1 \\ OH & 3, \\ OH & 5 \end{cases}$ is prepared by fusing 1, 3, 5-chlortoluene-sulphonic acid with caustic potash. By treatment with ammonia it absorbs oxygen from the air and is converted into *orcein*, $C_{28}H_{24}N_2O_7$, which dissolves in alkalies to form a dark-red dye. Orcein is used in histology. It is contained in the natural dye archil, which is prepared, like litmus, by exposing powdered lichens suspended in ammoniacal solution to the action of the air.

TRIACID PHENOLS.

Pyrogallol (*pyrogallic acid,* 1, 2, 3-phentriol) is 1, 2, 3-trihydroxybenzene, $C_6H_3(OH)_3$, and is prepared by the dry distillation of gallic acid (see exp. below):



$$C_6H_2\left\{\begin{matrix}(OH)_3\\ COOH\end{matrix}\right. = C_6H_3\left\{\begin{matrix}OH\ (1)\\ OH\ (2)\\ OH\ (3)\end{matrix}\right. + CO_2.$$

(Gallic acid) (Pyrogallol)

It forms fine needle-shaped crystals and is easily soluble in water. The solution when made alkaline greedily absorbs oxygen from the air, so that it is used for this purpose in gas analysis (see exp. below). Carbonates and acetates along with some carbon monoxide gas are produced by the oxidation. It is also extensively employed as a developer in photography.

Phloroglucinol (*phloroglucin,* 1, 3, 5-phentriol), $C_6H_3(OH)_3$, is 1, 3, 5-trihydroxybenzene, and is obtained by the action of caustic potash on *phloretin,* which is split off from the glucoside phloridzin (see p. 228) by boiling the latter with acids.

Phloroglucinol is also employed along with vanillin in alcoholic solution as an indicator (*Günzberg's reagent*) for free mineral acid. On evaporating a drop of this reagent mixed with the acid solution to dryness it gives a deep-red stain if mineral acid is present.

Experiments. (1) Carefully heat 5 gm. of dry gallic acid in a retort; carbon dioxide is evolved and pyrogallol sublimes. Test some of the latter with dilute ferric chloride solution; an intense blue-black colour is obtained.

(2) Put 1 gm. of pyrogallol into a dropping funnel, add 10 c.c. of strong NaOH solution, cork tightly, and shake vigorously for a few minutes. Immerse the stem of the funnel in a cylinder of water, open the cock, whereupon the water rises to take the place of the oxygen that has been absorbed.

(3) Test solutions of resorcinol and pyrocatechol with ferric chloride; colour reactions are obtained.

HEXACID PHENOL DERIVATIVE.

Inosite, $C_6H_{12}O_6$, is, according to its empirical formula, isomeric with the hexose sugars. Its chemical structure is, however, entirely different, for it is a benzene derivative having a hydrogen atom and a hydroxyl group attached to each carbon atom of the ring, $C_6H_6(OH)_6$, (hexahydroxybenzene). It is quite possible that this is a derivative of cyclohexane (see p. 235). It occurs in animal tissue, especially in muscle.

AROMATIC ALCOHOLS (AND ALDEHYDES).

Besides the above, we may also have hydroxy derivatives of benzene where the hydroxyl group, instead of replacing one of the hydrogens of the benzene nucleus, is connected with a side chain. The best example is

benzyl alcohol, $C_6H_5\cdot CH_2OH$, which is *phenyl carbinol.* In their reactions such alcohols differ entirely from phenols and indeed possess all the properties of fatty primary alcohols. Thus, benzyl alcohol can be prepared by boiling benzyl chloride for some time (6–8 hours) with water (*cf.* synthesis of methyl alcohol, p. 93):

$$\underset{\text{(Benzyl chloride)}}{C_6H_5CH_2}\boxed{Cl+H}OH = C_6H_5\cdot CH_2OH + HCl.$$

The Cl group, being in this case connected with a side chain and not with the benzene nucleus, is easily replaceable by OH. Benzyl alcohol may also be made by treating benzoic aldehyde (oil of bitter almonds) with nascent hydrogen:

$$\underset{\text{(Benzoic aldehyde)}}{C_6H_5\cdot CHO} + 2H = C_6H_5\cdot CH_2OH.$$

The reactions of this alcohol agree with those of fatty alcohols: oxidation yields first an aldehyde (benzaldehyde) and then an acid (benzoic); ethers, such as benzyl methyl ether ($C_6H_5\cdot CH_2O\cdot CH_3$), and ethereal salts, such as benzyl acetate ($C_6H_5CH_2\cdot OOCCH_3$), are easily obtained. There are also substitution products (which, however, are not obtained by direct treatment) where one or more of the H atoms of the nucleus are replaced, e.g., chlorbenzyl alcohol, $C_6H_4Cl\cdot CH_2OH$.

Benzyl alcohol, however, differs in many respects from aliphatic alcohols: for instance, it does not form an ester with sulphuric acid. Its boiling-point is 206.5°.

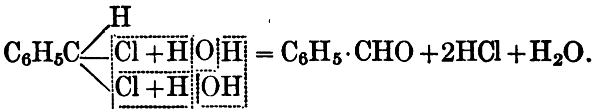
The *homologues* of benzyl alcohol are of two kinds: (*a*) those in which the phenyl group remains unchanged, but the alcoholic side chain contains some higher fatty radicle, and (*b*) those in which the alcoholic side chain remains unchanged (i.e., remains as carbinol), but one or more of the H atoms of the benzene nucleus become replaced by radicles, as in tolyl carbinol, $C_6H_4\begin{cases} CH_3 \\ CH_2OH \end{cases}$.

These alcohols, since they contain the primary alcohol group, can be oxidized to aldehydes and acids.

Benzoic aldehyde (benzaldehyde, oil of bitter almonds), $C_6H_5\cdot CHO$, is an important substance, being very reactive and therefore much employed for organic synthesis. Besides being produced by oxidation of benzyl alcohol, it can be obtained by the action of a hydrolyzing ferment—emulsin—on amygdalin, a glucoside contained in bitter almonds, the stone of the peach, etc. (see p. 228). The emulsin is usually present along with the amygdalin. Hydrocyanic acid is also produced during the reaction:

$$\underset{\text{(Amygdalin)}}{C_{20}H_{27}NO_{11}} + 2H_2O = \underset{\text{(Benzaldehyde)}}{C_6H_5\cdot CHO} + HCN + \underset{\text{(Dextrose)}}{2C_6H_{12}O_6}.$$

It can also be prepared by distilling a mixture of a benzoate and a formate, and by heating benzal chloride, $C_6H_5CHCl_2$, with water and milk of lime under pressure:



$$C_6H_5C\begin{cases} H \\ \boxed{Cl + H\,|\,O\,|\,H} \\ \boxed{Cl + H\,|\,OH} \end{cases} = C_6H_5\cdot CHO + 2HCl + H_2O.$$

It is an oil of a pleasant odour, boiling at 180° and having a specific gravity of 1.0504 at 15°. Although relatively insoluble in water, it is used as a flavouring agent. It is not poisonous. Like other aldehydes, it forms addition products with such substances as hydrocyanic acid and acid sulphites. It also combines with alcohols, acids, ketones, etc., and forms a hydrazone[1] (see p. 291) with phenylhydrazine. By boiling a solution of benzyl aldehyde in dilute alcohol containing some potassium cyanide, two molecules of it condense, forming *benzoin*, $C_6H_5 \cdot CHOH \cdot COC_6H_5$. In contact with air it readily oxidizes to benzoic acid, and with nascent hydrogen it combines to form benzyl alcohol. Like other aldehydes, it is a reducing agent; thus, it reduces ammoniacal $AgNO_3$ forming a mirror.

When benzaldehyde is treated with acetic anhydride, *benzoyl acetyl peroxide* is produced. This is called **acetozone** and is believed to have strong germicidal powers by virtue of being a peroxide. It is used therapeutically for intestinal disorders.

Any aromatic aldehyde when shaken with strong KOH and allowed to stand undergoes oxidation and reduction simultaneously, the product being equal quantities of alcohol (reduction) and acid (oxidation).

EXPERIMENTS. (1) To 5 c.c. of benzyl chloride (or benzoyl chloride) in a small flask add 50 c.c. of dilute lead nitrate solution. Attach to a reflux condenser and boil for ten minutes. Note the odour of benzaldehyde. Filter while very hot, add to the filtrate a gram of Na_2SO_4, then an equal volume of alcohol, cool and filter. Evaporate the filtrate almost to dryness on a water bath. Dissolve some of the moist yellowish residue in 2 c.c. of water in a test-tube, using heat. Pour this into some fuchsin aldehyde reagent (see p. 107). The colour is intensified on heating, because benzaldehyde is soluble in hot water, but only slightly soluble in cold water. Save the balance of the residue to secure benzoic acid (p. 275), for the oxidizing action really goes farther than the following equation shows:

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[1] Only the compounds formed from sugars with phenylhydrazine are called osazones (p. 216); those formed from other aldehydes or ketones are called hydrazones.

$$2C_6H_5 \cdot CH_2Cl + Pb(NO_3)_2 = \\ = 2C_6H_5 \cdot CHO + PbCl_2 + NO + NO_2 + H_2O.$$

(2) To some solution of phenylhydrazine in dilute acetic acid add a few drops of benzaldehyde. Collect the precipitate and crystallize it from alcohol. The crystals of hydrazone melt at 152°.

CHAPTER XXVI.

AROMATIC ACIDS.

MONOBASIC ACIDS.

Aromatic acids are in general analogous with those of the paraffins, being monobasic, dibasic, etc. The representative *monobasic* acid is **benzoic,** $C_6H_5 \cdot COOH$. This acid is of great commercial value and of much physiological interest, since, as will be explained later, it is the end product of the oxidation in the animal body of a large number of benzene derivatives having oxidizable side chains.

It can be prepared by numerous reactions, the most important of which are as follows:

1. By oxidation of *any* benzene derivative with a single fatty side chain. It follows from this that if an aromatic substance yields benzoic acid on oxidation, it must contain only one side chain. When two side chains exist a dibasic acid (phthalic) is obtained. Thus the hydrocarbons of the benzene series, $C_6H_5CH_3$, $C_6H_5C_2H_5$, $C_6H_5C_3H_7$, their monacid alcohols and aldehydes, $C_6H_5CH_2OH$, $C_6H_5CH_2CH_2OH$, C_6H_5CHO, etc., and their halogen derivatives where the halogen is situated in the side chain, all yield benzoic acid when oxidized.

2. By hydrolysis of benzonitrile, C_6H_5CN (see p. 156). The reagent can be obtained by substituting the CN group for an H of benzene, either by distilling potassium benzene sulphonate with potassium cyanide,

$$C_6H_5SO_3K + KCN = C_6H_5Cn + K_2SO_3,$$

or by heating a diazonium salt with $Cu_2(CN)_2$ (see p. 289).

3. By treating *benzoyl chloride* (see p. 276) with water,

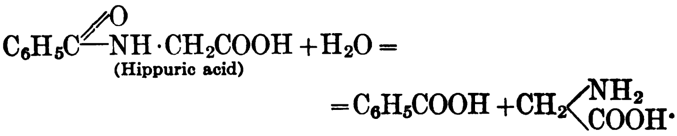
$$C_6H_5CO\boxed{Cl + H}OH.$$

4. Commercially, benzoic acid is obtained by treating boiling toluene with chlorine, whereby *benzotrichloride*, $C_6H_5CCl_3$, is produced, which is then boiled with water (see exp. below):

$$C_6H_5C\left\{\boxed{\begin{array}{ll} Cl & H \\ Cl + & H \\ Cl & H \end{array}}\ \boxed{\begin{array}{ll} O & H \\ O & H \\ O & H \end{array}}\right. = C_6H_5COOH + 3HCl + H_2O.$$

5. From gum benzoin by sublimation or treatment with alkalies.

6. By heating hippuric acid (see p. 277) with hydrochloric acid (hydrolysis):



$$C_6H_5C\overset{\displaystyle /\!\!/ O}{\diagdown}NH\cdot CH_2COOH + H_2O =$$
(Hippuric acid)
$$= C_6H_5COOH + CH_2\left\langle\begin{array}{l} NH_2 \\ COOH \end{array}\right. .$$

Benzoic acid forms needle-shaped crystals which melt at 121.3° (corrected) and readily sublime. Relatively insoluble in cold water, its solubility increases with rise in temperature until, at 90° C., the water contains 11.2% of the acid, and the crystals that remain undissolved melt and form a layer beneath the water. On further raising the temperature the two layers gradually mix till, at 116°, a homogeneous liquid is obtained. It is soluble in alcohol and ether, and volatilizes with steam. Its salts and derivatives are very numerous, and are analogous with those of acetic acid. Most of them are soluble in water.

Of the *metallic salts* those of sodium and ammonium are employed as medicines.

The *ethereal salts* are prepared in the same way as are those of acetic acid (see exp. (1) (*a*)).

EXPERIMENTS. (1) *Preparation of benzoic acid.* (*a*) Extract benzoic acid from the residue saved from the benzaldehyde experiment (see p. 272). Dissolve the residue with boiling water, filter while hot, and cool the filtrate. Collect the crystals of benzoic acid on a filter, wash with cold water, press between filter-paper. Make the *ethyl benzoate test* for benzoic acid as follows: To some of the dried benzoic acid add 1 c.c. of alcohol and about 3 c.c. of concentrated H_2SO_4. Heat; just as it begins to boil, notice the peppermint-like odour of ethyl benzoate.

(*b*) Put into a flask 5 c.c. of benzotrichloride, 100 c.c. of water, and small pieces of pumice. Attach to a reflux condenser and boil for two hours. Before cooling add 200 c.c. of hot water and filter at once. Cool, collect the crystals on a filter, recrystallize from hot water. and make the ethyl benzoate test on the dried crystals. Save a sample of benzoic acid.

(c) Heat together 1 c.c. of benzaldehyde and an excess of potassium permanganate solution until the odour of benzaldehyde is imperceptible. Add permanganate as required to maintain a pink colour. Decolorize with a few drops of alcohol. Cool, filter, and add HCl to the filtrate; benzoic acid crystallizes out:

$$C_6H_5CHO + O = C_6H_5COOH.$$

(2) Sublime benzoic acid from gum benzoin or from impure benzoic acid (see p. 12).

Benzoyl chloride, the acid chloride of benzoic acid, C_6H_5COCl, can be obtained by the action of chlorine on benzaldehyde, or by the action of PCl_5 on benzoic acid: $C_6H_5COOH + PCl_5 = C_6H_5COCl + POCl_3 + HCl$. It is more stable than acetyl chloride, not being decomposed by water in the cold. It resembles acetyl chloride, however, in that it reacts with the hydroxyl group of alcohols to form esters of benzoic acid. The presence of caustic alkali greatly facilitates this reaction. It reacts thus with the hydroxyl groups in dextrose, the resulting ester being insoluble in water and in dilute alkali.

EXPERIMENT. (a) Dissolve 1 c.c. of glycerol in 2 c.c. of water, add 4 c.c. of benzoyl chloride, and shake until the odour of the chloride has disappeared, in the meantime adding NaOH solution to maintain a slightly alkaline reaction. Glyceryl tribenzoate separates out. (b) Repeat (a), using a strong dextrose solution instead of glycerol solution.

The *substitution products* of benzoic acid are numerous, for of each there may be an ortho, meta, and para variety. They can be made by oxidizing the corresponding substituted toluenes, or by direct substitution of one or more of the hydrogens of the phenyl radicle in benzoic acid, by the same methods as are used for the substitution products of benzene. The chlorbenzoic acids, the nitrobenzoic acids, the aminobenzoic acids, and the sulphobenzoic acids are examples (see p. 306).

An important compound of benzoic acid, from a biochemical standpoint, is **hippuric acid.** This is benzoylaminoacetic acid, $C_6H_5CO \cdot NH \cdot CH_2COOH$. It is present in the urine of herbivorous animals, being produced in the kidney by a synthesis of glycin and benzoic acid. It also appears in human urine when benzoic acid is administered, or when foods yielding it in the organism are ingested. It may be prepared in the laboratory by several methods:

1. Heating glycocoll and benzoic acid to 160° in a closed tube.

2. Shaking glycin dissolved in sodium hydroxide solution with benzoyl chloride (see exp. below):

$$C_6H_5CO\boxed{Cl+H}HNCH_2COOH = \\ = C_6H_5CO \cdot NH \cdot CH_2COOH + HCl.$$

3. Heating *benzamide* with chloracetic acid (benzamide is analogous to acetamide, see p. 187):

$$C_6H_5CONH\boxed{H+Cl}CH_2COOH = \\ = C_6H_5CO \cdot NH \cdot CH_2COOH + HCl.$$

Hippuric acid is relatively insoluble in cold water, alcohol, and ether, and forms long rhombic crystals, having a melting-point of 190.3° (corrected). It is readily decomposed by boiling with acids or alkalies, and also decomposes when urine containing it undergoes fermentation.

EXPERIMENTS. (1) *Synthesize hippuric acid.* Shake together 1 c.c. of benzoyl chloride and a solution of 0.2 gm. of glycocoll in 10 c.c. of 10% NaOH. Add a few cubic centimetres of ether to dissolve the excess of benzoyl chloride, and shake until the aqueous liquid is colourless. Remove the bottom layer with a pipette, warm in an evaporating dish until odourless, and filter. Acidulate the filtrate with HCl. Collect the hippuric acid on a filter, wash with a little water, press dry between filter-paper, and complete the drying with a little alcohol-ether mixture. Save a sample. Test part of it as follows (exp. 2).

(2) (*a*) Test the solubility of hippuric acid in petroleum ether (compare benzoic acid). (*b*) Heat a little dry hippuric acid in a test-tube; benzoic acid sublimes, while the residue becomes reddish.

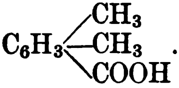
(3) Prepare hippuric acid from the urine of cows or horses, as follows: Evaporate the urine to one third its bulk. Add HCl; when cool, hippuric acid is deposited; filter, and recrystallize from dilute HNO_3. Make the above tests (exp. 2). Boil the remainder with concentrated HCl for fifteen minutes; on cooling, benzoic acid separates out. Test it for the latter (see p. 275).

Corresponding to *toluene* there are four monobasic **toluic acids.** Three of these (*o*-, *m*-, *p*-) have the formula $C_6H_4<\begin{matrix}CH_3\\COOH\end{matrix}$ and are made by oxidizing the corresponding xylenes with nitric acid. The fourth has the formula $C_6H_5CH_2COOH$ and might be called **phenyl-acetic acid.** It is obtained by treating benzyl chloride, $C_6H_5CH_2Cl$, with potassium cyanide and hydrolyzing he resulting nitrile ($C_6H_5CH_2CN$):

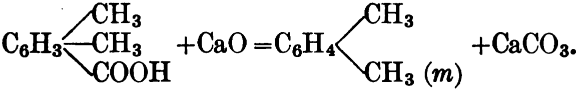
$$C_6H_5CH_2CN + 2H_2O = C_6H_5CH_2COOH + NH_3.$$

A homologue of this is phenyl-propionic or **hydro-cinnamic acid**, $C_6H_5CH_2CH_2COOH$.

Mesitylene yields only one acid, **mesitylenic,**



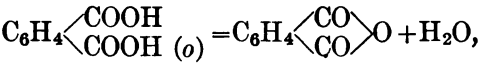
$C_6H_3\left\langle\begin{matrix}CH_3\\CH_3\\COOH\end{matrix}\right.$. This is of importance because it can be converted into metaxylene by distillation with lime (cf. benzene, p. 244):



$$C_6H_3\left\langle\begin{matrix}CH_3\\CH_3\\COOH\end{matrix}\right. + CaO = C_6H_4\left\langle\begin{matrix}CH_3\\ \\CH_3\ (m)\end{matrix}\right. + CaCO_3.$$

DIBASIC ACIDS.

In agreement with theory, there are three of these. They are called **phthalic acids.** Orthophthalic acid is prepared by oxidizing naphthalene (see p. 319) with sulphuric acid, or by oxidizing *o*-toluic acid with potassium permanganate. When heated it decomposes into water and an anhydride,



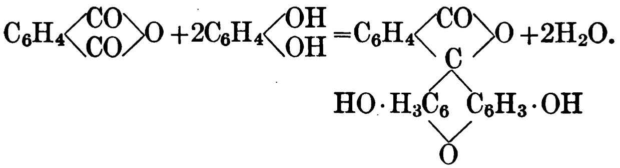
$$C_6H_4\left\langle\begin{matrix}COOH\\COOH\end{matrix}\right. (o) = C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle O + H_2O,$$

which latter, when heated with phenols in the presence of H_2SO_4, yields phenolphthalein (see exp. 3), a body of complicated structure used extensively as an indicator in volumetric analysis, being red in alkaline and colourless in acid solution (see p. 309).

The meta- and paraphthalic acids do not form anhydrides. Certain iodine derivatives of phenolphthalein, as *nosophen*, *eudoxine*, and *antinosine*, are used as medicines.

EXPERIMENTS. (1) Heat some phthalic acid in a sublimation apparatus (see p. 12); the sublimate is phthalic anhydride.

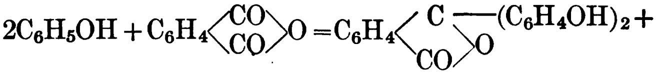
(2) To some phthalic anhydride add an equal quantity of resorcinol and 1 c.c. of concentrated H_2SO_4, then warm until deep red. Dilute with 100 c.c. of water and render alkaline with NaOH. The resulting solution of *fluoresceïn* is pinkish to transmitted light, but shows a marked greenish fluorescence to reflected light:



$$C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle O + 2C_6H_4\left\langle\begin{matrix}OH\\OH\end{matrix}\right. = C_6H_4\left\langle\begin{matrix}CO\\C\end{matrix}\right\rangle O + 2H_2O.$$
$$\begin{matrix}C\\ HO\cdot H_3C_6 \quad C_6H_3\cdot OH\\ O\end{matrix}$$

(Fluoresceïn)

(3) Mix equal quantities of phthalic anhydride and phenol, add a little C.P. H_2SO_4, and warm until strongly coloured. Pour into a large quantity of water. This solution of phenolphthalein becomes red when it is made faintly alkaline:



$$2C_6H_5OH + C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle O = C_6H_4\left\langle\begin{matrix}C\text{---}(C_6H_4OH)_2\\CO\end{matrix}\right\rangle O + H_2O.$$

(Phenolphthalein)

$+H_2O.$

There is a *hexabasic* acid, viz., **mellitic,** $C_6(COOH)_6$, which is found in nature in combination with aluminium as the mineral mellite.

CHAPTER XXVII.

AROMATIC NITROGEN AND SULPHUR DERIVATIVES.

THERE is very little similarity between the nitrogen compounds of the aromatic bodies and those of the paraffins. The nitro compounds of the paraffins we have seen to be of little importance; those of the aromatic bodies, on the other hand, are of prime importance, because they are readily produced and are easily converted into other nitrogenous derivatives. On this account *nitration* forms the first step in many organic syntheses.

NITRO COMPOUNDS.

By shaking benzene in the cold with a mixture of pure nitric and sulphuric acids, **mononitrobenzene,** an oily liquid boiling at 206°–207°, is obtained.[1] The sulphuric acid absorbs the water produced: $C_6H_6 + HNO_3 = C_6H_5NO_2 + H_2O$ (Compare with nitro compounds of paraffins, p. 162.)

EXPERIMENT. To 80 c.c. H_2SO_4 in a flask add, while shaking, 70 c.c. of colourless HNO_3. Cool thoroughly. Add (a little at a time) 20 c.c. of benzene, keeping the temperature of the mixture below 30° and shaking frequently. Attach a vertical air-condenser tube; heat for an hour in a bath kept at 60°, shaking occasionally. Cool, pour into a separating funnel, draw off the bottom layer of acid, and wash the oil several times with water (the nitrobenzene becomes the bottom layer). Warm with dry calcium chloride in a flask on a water-bath until the liquid becomes clear. Distil in a fractionating flask, using an air-condenser, and observe the boiling-point. Note the odour of the distillate.

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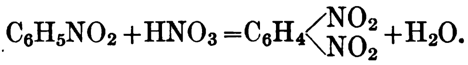
[1] Mononitrobenzene has the odour of bitter almonds and is known as essence of mirbane. It is poisonous.

If, on the other hand, the reaction be allowed to proceed at boiling temperature and with fuming nitric acid the product is **dinitrobenzene,** a crystalline substance melting at 90° (corrected):



$$C_6H_5NO_2 + HNO_3 = C_6H_4\left\langle\begin{matrix}NO_2\\NO_2\end{matrix}\right. + H_2O.$$

Three varieties of this are possible (see p. 248).

EXPERIMENT.—*Prepare dinitrobenzene (meta).* Mix in a beaker 25 c.c. of C.P. H_2SO_4 and 25 c.c. of fuming HNO_3. Immediately add very slowly 5 c.c. of benzene from a pipette. After the action subsides, boil for a while and then pour the mixture into 250 c.c. of cold water. Filter off the precipitate, press between filter-paper, and crystallize from alcohol. Make a melting-point determination with dried crystals. Save a sample of the crystals.

Toluene and the xylenes react with nitric acid in the same manner. In fact, the more alkyl groups there are attached to the benzene nucleus, the more easily can nitro groups be introduced into it. The nitro compounds are very stable.

AMINO COMPOUNDS.

The most important reaction of nitro compounds is with nascent hydrogen, whereby they become converted into amino compounds, of which **aniline** (phenylamine) is the representative:

$$C_6H_5NO_2 + 6H = \underset{\text{(Aniline)}}{C_6H_5NH_2} + 2H_2O.$$

Commercially, aniline is produced by mixing nitrobenzene with iron filings and hydrochloric acid in an iron cylinder provided with a stirring apparatus, and, when the action is over, adding lime and distilling the aniline. It is a colourless liquid, boiling at 183.7° (corrected); its specific gravity at 16° is 1.024. If not perfectly pure it becomes coloured on standing. It is soluble in about 30 parts of water, and one part of water is soluble in about 20 parts of aniline. It is readily soluble in alcohol. It gives several important colour reactions, described in the experiments below. It may be considered as NH_3 in which one H is displaced by C_6H_5. Like all such bodies (see p. 157), it directly combines with acids to form (aniline) salts, e.g., $C_6H_5NH_2 \cdot HCl$; $C_6H_5NH_2 \cdot HNO_3$; $C_6H_5NH_2 \cdot H_2SO_4$. The hydrochloride is technically known as *aniline salt.* In watery solution, however, aniline is not alkaline towards litmus and scarcely conducts an electrical current; in other words, it does not become ionized (see p. 51). It is, therefore, quite different in this respect from aliphatic amines, which with water form bases, some of which are stronger even than ammonia (*cf.* p. 160). Phenyl (C_6H_5) diminishes the basic properties of the amino (NH_2) group, whereas fatty residues increase the basic properties of NH_2.

Aniline can be liberated from the acid in its salts by distilling with caustic alkali:

$$C_6H_5NH_2 \cdot HCl + KOH = C_6H_5NH_2 + KCl + H_2O.$$

It can also be obtained by distilling indigo (hence its name, *anil* being the Spanish for indigo). It is an extremely important substance in organic synthesis.

EXPERIMENTS. (1) *Preparation of aniline.* Put 30 gm. of granulated tin and 20 c.c. of nitrobenzene into a large flask, add gradually (in portions of 5 c.c. each) 65 c.c. of C.P. HCl, and cool the flask whenever the action becomes very vigorous. When all the acid has been added, heat on a water bath for one hour, using a vertical air-condenser. Now dilute with 50 c.c. of water, add 50% NaOH until strongly alkaline and until the stannic oxide redissolves; cool the flask if the mixture boils. Distil with steam. When the distillate comes clear, stop the process. Add to the distillate 25 gm. NaCl for each 100 c.c.; shake in a separating funnel with three portions of 10 c.c. of chloroform. Dry the filtered chloroform extract with anhydrous potassium carbonate. Next empty the liquid into a fractionating flask, distil off the chloroform, then distil the aniline, using an air-condenser.

(2) *Tests.* (*a*) Dissolve a *little* $KClO_3$ in 0.5 c.c. H_2SO_4; add a few drops of aniline solution—a blue-violet colour appears; dilute with water—the colour changes to red; then add ammonia, and the blue is

restored. (*b*) To a solution of aniline in H_2SO_4 add a few drops of potassium dichromate solution—a blue colour appears. (*c*) To some aniline solution (in water) add a filtered solution of bleaching-powder—a purple colour develops.

Derivatives of Aniline. The *homologues* include three **toluidines,** of which the ortho and para varieties are important, and six **xylidines,** this large number of isomers being due to differences in the relative positions of the amido and methyl groups. When a mixture of aniline and the toluidines is treated with oxidizing agents a compound known as **rosaniline** is obtained. This is the mother substance of the aniline dyes. Rosaniline is $(NH_2C_6H_4)_2C(OH)C_6H_3\Big\langle\begin{smallmatrix}CH_3\\NH_2\end{smallmatrix}$. *Fuchsin* is rosaniline hydrochloride.

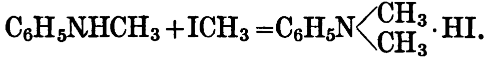
EXPERIMENT. Heat together in a test-tube 1 c.c. of aniline, 1 gm. of paratoluidine, and 0.5 gm. $HgCl_2$ until dark red in colour. Cool partly, dissolve in alcohol; a deep-red fuchsin colour appears.

Replacement of one or more of the H atoms of the NH_2 group in aniline can be effected in various ways.

By reaction with alkyl halides secondary and tertiary *mixed aromatic fatty amines* are obtained. Thus with methyl iodide, methyl aniline and dimethyl aniline are produced:

$$C_6H_5NH\boxed{H+I}CH_3 = C_6H_5NHCH_3\cdot HI$$

and

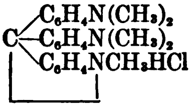


$$C_6H_5NHCH_3 + ICH_3 = C_6H_5N\Big\langle\begin{smallmatrix}CH_3\\CH_3\end{smallmatrix}\cdot HI.$$

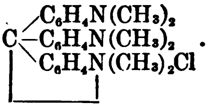
Some quaternary base is also formed by the reaction.

Dimethyl aniline is commercially the most important of these mixed amines and is prepared by heating aniline hydrochloride with methyl alcohol, methyl chloride being first formed, which then reacts as above.

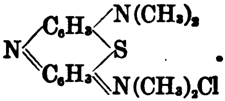
Dimethyl aniline + chloranil ($C_6Cl_4O_2$) gives **methyl violet,** which is a mixture of two salts with the following formulæ:



and



Methyl violet is also called *pyoktanin.* **Methylene blue** (methylthionin hydrochloride) has the formula



In a similar manner replacement with phenyl groups may occur, di- and triphenylamine being produced.

Diphenylamine, $C_6H_5NHC_6H_5$, is obtained by heating aniline with aniline hydrochloride to 200°:

$$C_6H_5NH\boxed{H+HClNH_2}C_6H_5=C_6H_5NHC_6H_5+NH_4Cl.$$

With acid chlorides, aniline forms *anilides,* which are analogous with the acid amides (see p. 186):

$$CH_3CO\boxed{Cl+H}HNC_6H_5=\underset{\text{(Acetanilide)}}{CH_3COHNC_6H_5}+HCl.$$

One of these, **acetanilide** (phenylacetamide), is of very great therapeutic interest on account of its antipyretic properties. It is the active drug in many proprietary headache medicines (antikamnia, antifebrine, orangine powders, etc.). These remedies are not entirely harmless, since acetanilide acts as a circulatory depressant. Acetanilide is easily prepared by heating aniline with glacial acetic acid (see exp.):

$$C_6H_5NH\boxed{H+HO}OCCH_3 = \underset{\text{(Acetanilide)}}{C_6H_5\cdot NH\cdot OCCH_3} + H_2O.$$

Experiment. Mix 10 c.c. each of aniline and glacial acetic acid in a small flask attached to a reflux condenser; boil for four hours. Dilute with 100 c.c. of boiling water and filter at once, using a hot funnel. On cooling, acetanilide crystallizes out. Recrystallize from hot water. Save a sample.

Acetanilide is very slightly soluble in water and crystallizes from it in colourless plates. It melts at 114.2° (corrected). Two other antipyretic drugs are closely related to acetanilide. In one of these, **exalgin** (methyl acetanilide), the hydrogen atom of the amido group is replaced by methyl, $C_6H_5NCH_3COCH_3$. In the other, **benzanilide** (benzoyl anilide), the acetyl radicle is replaced by benzoyl, $C_6H_5\cdot NH\cdot OCC_6H_5$.[1]

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[1] In their passage through the animal body these drugs become partially oxidized to aminophenol $C_6H_4\left\langle\begin{matrix}OH\\NH_2\end{matrix}\right.$, which also has antipyretic properties, and it has been thought that it is really this substance which produces the antipyretic action. On this supposition, various derivatives of paraminophenol have been prepared and found to be equally active as antipyretics. These will be described later on (p. 297). Acetyl paraminophenol as well as aminophenol is produced in the animal body.

DIAZO COMPOUNDS.

When fatty amino derivatives are treated with nitrous acid, nitrogen is evolved and a hydroxyl group takes the place of the amino group; with the aromatic amines, on the other hand, nitrous acid at low temperatures has quite a different action. It converts them into **diazo compounds,** so called because they contain two nitrogen (nitrogen =*azote* (French)) atoms linked together. The diazo compounds are of very great importance in organic synthesis on account of the readiness with which they can be converted into other bodies. They are prepared by treating an ice-cold solution of an aniline salt with nitrous acid or with ethyl nitrite:

$$C_6H_5NH_2HNO_3 + HNO_2 = \underset{\text{(Benzene diazonium nitrate)}}{C_6H_5N{=}NNO_3} + 2H_2O.$$

If a diazonium salt be dried and struck with a hammer it explodes. Its most important reactions are as follows:

1. *With water* it forms phenol and nitrogen (see exp. (2) (*b*):

$$C_6H_5N{=}NCl + H_2O = C_6H_5OH + N_2 + HCl.$$

To obtain this result the diazonium salt is best prepared by treating a cold, acidified solution of an aniline salt with an equivalent quantity of sodium nitrite, and then boiling (see exp. 2, p. 259).

2. Boiling *with alcohol* causes replacement of the diazo group either by ethoxy ($—O—C_2H_5$) or hydrogen. In the first case phenyl ethyl ether or *phenetole* is formed:

$$C_6H_5N{=}NCl + C_2H_5OH = C_6H_5OC_2H_5 + N_2 + HCl.$$

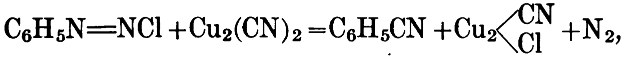
In the second case benzene and aldehyde:

$$C_6H_5N{=}NCl + C_2H_5OH = C_6H_6 + CH_3CHO + N_2 + HCl.$$

3. Heating *with a halogen acid* or, better still, with an acid solution of the corresponding cuprous salt of the acid causes replacement of the diazo group by the halogen:

$$C_6H_5N{=}NCl + HCl = C_6H_5Cl + N_2 + HCl:$$

4. Heating *with cuprous cyanide* replaces the diazo group by cyanogen:



$$C_6H_5N{=}NCl + Cu_2(CN)_2 = C_6H_5CN + Cu_2{<}\genfrac{}{}{0pt}{}{CN}{Cl} + N_2,$$

and the resulting nitrile can be hydrolyzed to form benzoic acid (see p. 274).

Other replacements by hydrocarbon residues, sulphur groups, etc., can also be effected.

EXPERIMENTS. (1) Prepare benzene diazonium nitrate. Put 50 gm. of arsenic trioxide into a flask; provide a funnel-tube, as in other gas-generators, and a delivery-tube which is connected with an empty bottle or cylinder standing in cold water. Mix 10 gm. of aniline nitrate with 12 c.c. of cold water in a graduate or large test-tube standing in ice-water, and immerse in the liquid a delivery-tube coming from the condenser-bottle of the gas apparatus. Through the funnel add 50 c.c. of concentrated HNO_3 to the As_2O_3; heat as is necessary to keep up an evolution of nitrogen oxides. Bubble the gas into the aniline nitrate mixture until complete solution is secured. Add to the solution an equal volume of alcohol cooled to 0°, then some cold ether. An abundant precipitate of benzene diazonium nitrate is obtained. Filter quickly with suction. Test for the following reactions at once:

(2) (*a*) Dissolve some in water and let it stand. It decomposes, as is shown by change of colour. (*b*) Boil some with water; notice the phenol odour. (*c*) Boil some with alcohol in a test-tube; it is decomposed with production of phenetole. (*d*) Add some to a little concentrated HCl and boil. Chlorbenzene is formed; on adding water this sinks to the bottom. (*e*) The dried salt is explosive; place a small particle on a piece of iron and strike it with a hammer.

In all the above cases the N_2 group is replaced. Diazo compounds, however, exhibit another type of reaction in which the N_2 group is retained and a new substance of greater stability is produced. The more important of these substances are:

a. **Diazoamino Compounds.** In these, one of the hydrogens of an amido group is replaced by a diazo residue. A type of the class is *diazoaminobenzene*, $C_6H_5 \cdot N{=}N \cdot NH \cdot C_6H_5$, which is prepared by bringing together aniline and diazonium chloride in neutral solution. It forms yellowish crystals, which are insoluble in water but soluble in alcohol. By heating with aniline, and in various other ways, diazoaminobenzene becomes converted by a rearrangement of atoms into

b. **Aminoazobenzene,** $C_6H_5 \cdot N{=}N \cdot C_6H_4 \cdot NH_2$, which is the amino derivative of a substance called azobenzene.

Dimethyl aminoazobenzene is $C_6H_5 \cdot N_2 \cdot C_6H_4 \cdot N(CH_3)_2$. It is used as an indicator for free acid, giving a pink colour in the presence of the latter (see p. 312).

c. **Azobenzene,** $C_6H_5 \cdot N{=}N \cdot C_6H_5$. Azobenzene can be obtained by partial reduction of nitrobenzene. It forms orange-red crystals and is soluble in water, but the resulting solution is not a dye (see p. 315). The azo group is present, however, in many dyes.

d. **Hydrazobenzene,** $C_6H_5NH{-}NHC_6H_5$, is obtained by reducing azobenzene; it is colourless. Hydrazobenzene is the diphenyl derivative of *hydrazine*, $NH_2{-}NH_2$. The most important hydrazine derivative is

e. **Phenylhydrazine,** $C_6H_5NH{-}NH_2$, which forms hydrazones (see p. 271) with aldehydes, and osazones with sugars (see p. 216). It is obtained by reduction of diazonium salts (see exp.):

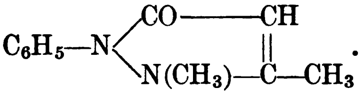
$$C_6H_5N_2Cl + 4H = \underset{\text{(Phenylhydrazine hydrochloride)}}{C_6H_5NH{-}NH_2 \cdot HCl.}$$

Experiment. To 10 c.c. of freshly distilled aniline add, while stirring, 100 c.c. of concentrated HCl. Cool, then add slowly from a dropping funnel a solution of sodium nitrite (10 gm. in 50 c.c. of water), until testing with starch-potassium-iodide paper shows the presence of free nitrous acid (blue colour). For the test dilute a drop of the acid mixture with 5 c.c. of water. Add a cold solution of 60 gm. of stannous chloride in 50 c.c. of concentrated HCl. Cool until a paste of crystals appears. Filter through muslin, using suction. Transfer to a porous plate, press out the phenylhydrazine hydrochloride crystals in a thin layer, and set away to dry out:

1. $C_6H_5NH_2 \cdot HCl + HNO_2 = C_6H_5N_2Cl + 2H_2O$.
2. $C_6H_5N_2Cl + 4H = C_6H_5NH \cdot NH_2 \cdot HCl$.

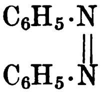
Free phenylhydrazine may be extracted by treating the hydrochloride with an excess of NaOH solution and shaking with ether. After dehydrating the ethereal extract, evaporate the ether; phenylhydrazine remains behind as a liquid which readily solidifies on cooling.

Phenylhydrazine is a colourless oil at ordinary temperature and boils at 243.5°, meanwhile undergoing some decomposition. It becomes dark on exposure to air. Its salts, e.g., the hydrochloride, are solid and are sometimes employed in place of the base itself for producing osazone crystals, the hydrochloric acid being neutralized by sodium acetate. By a series of reactions, which are too complicated for description here, a derivative of phenylhydrazine can be obtained which lowers fever temperature. This is **antipyrin** or **phenazone** (1-phenyl-2, 3-dimethyl pyrazolone),



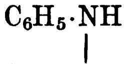
The relationship of these bodies to nitrobenzene and aniline will be evident from an examination of the following formulæ:

$C_6H_5NO_2$
(Nitrobenzene)



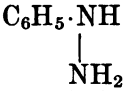
$$\begin{array}{c} C_6H_5\cdot N \\ \| \\ C_6H_5\cdot N \end{array}$$

(Azobenzene)



$$\begin{array}{c} C_6H_5\cdot NH \\ | \\ C_6H_5\cdot NH \end{array}$$

(Hydrazobenzene)



$$\begin{array}{c} C_6H_5\cdot NH \\ | \\ NH_2 \end{array}$$

(Phenylhydrazine)

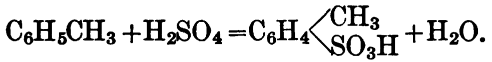
$C_6H_5NH_2$
(Aniline)

SULPHUR DERIVATIVES.

Sulphonic acids. With sulphuric acid the benzenes form sulphonic acids, thus:

$$C_6H_6 + H_2SO_4 = \underset{\text{(Benzene-sulphonic acid)}}{C_6H_5SO_3H} + H_2O$$

and



$$C_6H_5CH_3 + H_2SO_4 = \underset{\text{(Toluene-sulphonic acid)}}{C_6H_4\begin{matrix} CH_3 \\ SO_3H \end{matrix}} + H_2O.$$

It is of importance to note that in this respect they behave quite differently from paraffins. When an alkyl group (as in toluene), an amino group (as in aniline), or a hydroxyl group (as in phenol) is attached to the benzene nucleus, the sulphonic acid derivative is more easily formed than when benzene alone, or any of its other derivatives, is used.

The sulphonic acids are soluble in water and are strong acids, so that their salts are very stable, e.g., $C_6H_5SO_3Na$. Treated with phosphorus pentachloride the salts of sulphonic acids form sulphonic chlorides, which may be reduced to mercaptans:

1. $C_6H_5SO_3Na + PCl_5 = C_6H_5SO_2Cl + POCl_3 + NaCl.$
2. $C_6H_5SO_2Cl + 6H = \underset{\text{(Thiophenol)}}{C_6H_5SH} + HCl + 2H_2O.$

These reactions show us that sulphonic acids must possess an —OH group and that the S atom is in immediate connection with the benzene ring. The structural formula of benzene-sulphonic acid must therefore be $\begin{matrix} C_6H_5 \\ HO \end{matrix}\!>SO_2$, or sulphuric acid, $\begin{matrix} HO \\ HO \end{matrix}\!>SO_2$, in which one hydroxyl group is replaced by phenyl (*cf.* p. 163).

They give several other reactions, the following of which are important:

1. *Fused with potassium hydroxide*, benzene-sulphonic acid yields phenol,

$$C_6H_5SO_3K + KOH = C_6H_5OH + K_2SO_3.$$

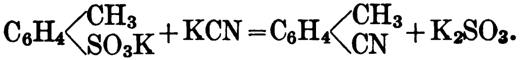
EXPERIMENTS. (1) To 75 gm. of fuming H_2SO_4 in a small flask to which an air-condenser is attached, add, a little at a time, 20 gm. of benzene, shaking and cooling after each addition. Transfer to a dropping funnel, and run the mixture out, drop by drop, into 300 c.c. of cold saturated NaCl solution. Keep the salt solution cold with ice-water. On standing, crystals of sodium benzene sulphonate form. Crystallization may be hastened by strongly cooling some of the mixture in a test-tube and emptying the crystalline mass into the main liquid. Filter the pasty mass of crystals with suction and wash it with a little saturated salt solution. Press dry, and complete the drying in an oven at 110°.

(2) Weigh the dry powder (of 1); weigh out five times as much KOH. Put the KOH in an iron dish, add a few cubic centimetres of water, and melt. Then add slowly, while stirring with a spatula, the sodium benzene sulphonate. Keep fused for an hour. Dissolve in water, acidulate with HCl, shake with ether, and treat the ethereal solution of phenol in the same way as in the previous phenol experiments (see p. 259).

2. *Distilled with potassium cyanide*, cyanides are formed:

$$C_6H_5SO_3K + KCN = C_6H_5CN + K_2SO_3$$

and



$$C_6H_4{<}\begin{matrix}CH_3\\SO_3K\end{matrix} + KCN = C_6H_4{<}\begin{matrix}CH_3\\CN\end{matrix} + K_2SO_3.$$

By hydrolysis these cyanides can be converted into acids:

$$C_6H_5CN + 2H_2O = C_6H_5COOH + NH_3.$$

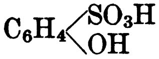
The toluene-sulphonic acids may be ortho or para. The meta variety is rare. The sulphonic acid group is present in many dyestuffs (see p. 315).

CHAPTER XXVIII.

MIXED AROMATIC COMPOUNDS.

HYDROXY COMPOUNDS.

INCLUDED under this head, we will consider certain compounds in which two or more dissimilar groups are attached to the benzene ring. It is evident that compounds of this nature must be extremely numerous. It will, of course, be possible here merely to indicate in a general way the more important of these. Besides the derivatives of the homologues of benzene which have already been described, the following are the most important mixed compounds:

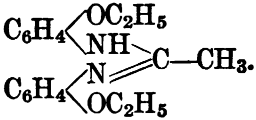
1. **Phenol and sulphonic groups** exist in phenol-sulphonic acid,  $C_6H_4\begin{smallmatrix}SO_3H\\OH\end{smallmatrix}$ (*o* or *p*), which is commercially known as *aseptol* and used as a disinfectant. The sodium salt of it is *sodium sulphocarbolate,* and is used to arrest fermentation in the stomach.

2. **Phenol and nitro groups** exist in mono- and trinitrophenol (picric acid), which have already been described (p. 262).

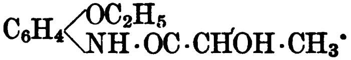
3. **Phenol and amino groups** exist in the aminophenols, which are prepared by reducing the mononitrophenols. The *para* variety is of therapeutic inter-

est. Its ethyl ether is known as *paraphenetidin*, $C_6H_4\left\langle\begin{matrix}OC_2H_5\\NH_2\end{matrix}\right.$, and if this is treated with glacial acetic acid, acetaminophenetole is formed, $C_6H_4\left\{\begin{matrix}OC_2H_5\\NH\cdot OCCH_3\end{matrix}\right.$, which is known in medicine as **phenacetin** (or acetphenetidin) and is perhaps the safest antipyretic. Phenacetin is a white crystalline substance, sparingly soluble in water and with a melting-point of 135°.

A number of other phenetidin derivatives are used in medicine, particularly holocain, lactophenin, and phenocoll. **Holocain** is

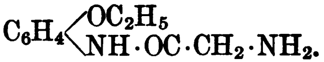


Lactophenin is lactylphenetidin,



$$C_6H_4\left\langle\begin{matrix}OC_2H_5\\NH\cdot OC\cdot CHOH\cdot CH_3\end{matrix}\right.\cdot$$

Phenocoll is aminoacetphenetidin,



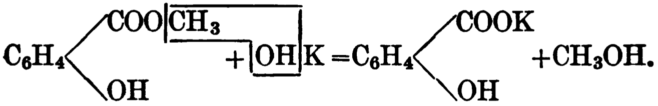
$$C_6H_4\left\langle\begin{matrix}OC_2H_5\\NH\cdot OC\cdot CH_2\cdot NH_2.\end{matrix}\right.$$

4. **Phenol and a primary alcohol group** are combined in saligenin, $C_6H_4\left\langle\begin{matrix}OH\\CH_2OH\end{matrix}\right.\cdot$ This exists in combination with dextrose in the glucoside **salicin** (see p. 228).

5. **An acid group** may exist along **with one or more hydroxyl groups.** According to the number of the latter groups we may have mono-, di-, and trihydroxybenzoic acids.

A. *Monohydroxybenzoic acids*, $C_6H_4\left<\begin{matrix}OH\\COOH\end{matrix}\right.$. The *ortho* variety of this is **salicylic acid**, an extremely important medicinal substance. It may be prepared by a variety of reactions, the chief of which are as follows:

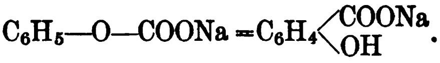
(1) By saponifying methyl salicylate (oil of wintergreen) with caustic potash:



$$C_6H_4\left<\begin{matrix}COO\boxed{CH_3}\\OH\end{matrix}\right. + \boxed{OH}K = C_6H_4\left<\begin{matrix}COOK\\OH\end{matrix}\right. + CH_3OH.$$

The potassium salicylate thus formed can be decomposed by acidifying with hydrochloric acid (see exp. 1, below).

(2) By subjecting sodium phenolate to the action of carbon dioxide, sodium phenyl carbonate, $C_6H_5OCOONa$, is formed, which, by heating to 130° C. in an autoclave, becomes converted into sodium salicylate:



$$C_6H_5—O—COONa = C_6H_4\left<\begin{matrix}COONa\\OH\end{matrix}\right. .$$

This method is used commercially.

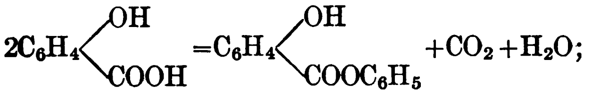
(3) By fusing orthotoluene-sulphonic acid, orthocresol, or orthosulphobenzoic acid with caustic potash. In the case of the first two bodies oxidation of the methyl side chain occurs. The replacement of the sulphonic group by hydroxyl has already been explained (*cf.* p. 258).

(4) By converting orthoaminobenzoic acid into the diazonium salt and boiling this with water (see p. 288).

Salicylic acid crystallizes in needles and melts at 159° (corrected). It is readily soluble in hot water, but only sparingly so in cold. Its aqueous solutions give an intense violet colour with ferric chloride. It is readily soluble in fat-solvents. Solutions of salicylic acid possess antiseptic properties, and, having no odour, it is therefore employed for preserving wines, foods, etc. Its sodium salt, $C_6H_4\Big\langle\begin{matrix}COONa\\OH\end{matrix}$, has great medicinal value in the treatment of rheumatism.

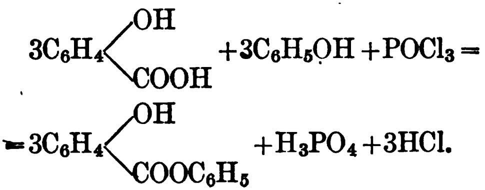
There are also *meta* and *para* hydroxybenzoic acids, which can be prepared from the corresponding amino- or sulphonic-benzoic acids. They do not react with ferric chloride.

Salicylic acid forms various salts, the salicylates, many of which are important. **Methyl salicylate,** $C_6H_4\Big\langle\begin{matrix}OH\\COOCH_3\end{matrix}$, is the chief constituent of oil of wintergreen. It can be made synthetically by heating methyl alcohol with sulphuric acid and salicylic acid. A very interesting compound of salicylic acid is phenyl salicylate, $C_6H_4\Big\langle\begin{matrix}OH\\COOC_6H_5\end{matrix}$, or **salol.** It is produced by heating salicylic acid alone to 200°–220° (see exp.).



$$2C_6H_4\Big\langle\begin{matrix}OH\\COOH\end{matrix}=C_6H_4\Big\langle\begin{matrix}OH\\COOC_6H_5\end{matrix}+CO_2+H_2O;$$

or by heating phenol and salicylic acid in the presence of phosphorus oxychloride:



$$3C_6H_4\Big\langle\begin{matrix}OH\\COOH\end{matrix}+3C_6H_5OH+POCl_3=$$
$$=3C_6H_4\Big\langle\begin{matrix}OH\\COOC_6H_5\end{matrix}+H_3PO_4+3HCl.$$

Salol is a white crystalline powder, somewhat aromatic in odour and melting at 43°. It is insoluble in water and unaffected by dilute acids. Alkalies readily saponify it, however, and yield salicylate and phenol. Taken internally it will therefore remain undecomposed till it reaches the intestine, when the phenol and salicylate liberated by action of the alkali will act as antiseptics. On this account it is used for intestinal antisepsis.

By the action of sulphuric acid on salicylic acid, **salicyl-sulphonic acid,** $C_6H_4\left\langle\begin{matrix}COOH\\OSO_3H\end{matrix}\right.$, is formed. This is a white crystalline deliquescent substance, readily soluble in water, the solution being a valuable precipitant for certain but not all proteids. Its solutions on standing become coloured.

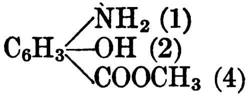
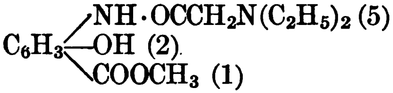
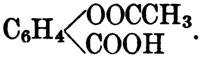
EXPERIMENTS. *Salicylic acid.* (1) Saponify 5 c.c. of oil of wintergreen by boiling with 100 c.c. of 20% NaOH, using a reflux condenser, until the oil has disappeared. Cool, acidulate with HCl, collect the crystals on a filter, and wash them with a small quantity of water. Dissolve the salicylic acid in a little hot alcohol, and filter the solution into a beaker half full of cold water. Collect the crystals.

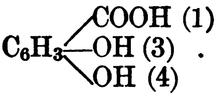
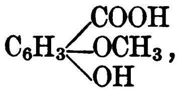
(2) Tests. (*a*) Add ferric chloride solution to some salicylic acid solution—violet-blue colour. Compare the similar phenol test. Try ferric chloride with alcoholic solutions of phenol and of salicylic acid. (*b*) Mix a little salicylic acid with some soda-lime and heat in a dry test-tube until the odour of phenol is noticed.

(3) *Prepare salol* as follows: Fill a dry test-tube

one third full of salicylic acid, fit the test-tube with a cork having a piece of small glass tubing 8 inches long passing through it, now heat gradually, boil the melted salicylic acid for five minutes, and, removing the cork, pour the hot liquid into some cold water in a beaker. Collect the insoluble material, heat it with some water in a test-tube, when it soon melts and sinks as dark-coloured drops. Decant off the water, add 2 c.c. of H_2SO_4; on heating a reddish colour develops.

There are several derivatives of salicylic acid among the newer remedies, as **sanoform** or diiodomethyl salicylate, **salophen** or acetyl-paraminophenyl salicylate, and **salipyrin**, a combination of salicylic acid with antipyrin.

Orthoform is the methyl ester of aminohydroxybenzoic acid,  $C_6H_3{<}\begin{matrix}NH_2\ (1)\\ OH\ (2)\\ COOCH_3\ (4)\end{matrix}$. **Nirvanin** is the methyl ester of diethylglycocoll-aminosalicylic acid,  $C_6H_3{<}\begin{matrix}NH\cdot OCCH_2N(C_2H_5)_2\ (5)\\ OH\ (2)\\ COOCH_3\ (1)\end{matrix}$. **Aspirin** is acetylsalicylic acid,  $C_6H_4{<}\begin{matrix}OOCCH_3\\ COOH\end{matrix}$. **Betol** is the naphthol ester of salicylic acid, $C_6H_4(OH)COO\cdot C_{10}H_7$.

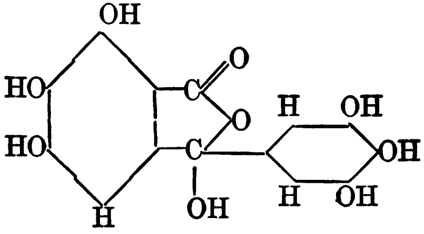
B. *Dihydroxybenzoic acid* is **protocatechuic,**  $C_6H_3{<}\begin{matrix}COOH\ (1)\\ OH\ (3)\\ OH\ (4)\end{matrix}$. Its monomethyl ether,  $C_6H_3{<}\begin{matrix}COOH\\ OCH_3\\ OH\end{matrix}$, is vanillic acid, which is derived from vanillin, the corresponding aldehyde, $C_6H_3\left\langle\begin{array}{l}CHO\\OCH_3\\OH\end{array}\right.$, by oxidation. **Vanillin,** contained in the vanilla-bean, is extensively employed as a flavouring agent. It is used, with phloroglucin, as an indicator for free mineral acid (see p. 312), (Synthetically it can also be prepared by treating guaiacol, $C_6H_4\left\langle\begin{array}{l}OCH_3\\OH\ (o)\end{array}\right.$, with chloroform and **caustic** soda.)

C. *Trihydroxybenzoic acid* is the important compound **gallic acid,** $C_6H_2\left\{\begin{array}{l}COOH\ (1)\\OH\ (3)\\OH\ (4)\\OH\ (5)\end{array}\right.(+H_2O)$. This is contained in certain plants, but is most readily obtained by boiling tannin with dilute mineral acid, or by fermenting gall-nuts. **Tannic acid** consists of two molecules of gallic acid minus one molecule of water; it is therefore a condensation product.

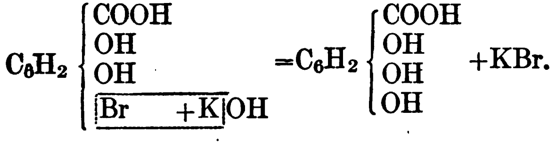
Tannic acid will be seen to bear a similar relation to gallic acid as disaccharides bear to monosaccharides:

$$\underset{\text{(Tannic acid)}}{C_{14}H_{10}O_9}+H_2O=\underset{\text{(Gallic acid)}}{2C_7H_6O_5}.$$

The following structural formula has been proposed for tannic acid:



That gallic acid has the structural formula given to it above is proved by the fact that it can be prepared by fusing bromprotocatechuic acid with KOH:



$$C_6H_2\left\{\begin{matrix}COOH\\OH\\OH\\\boxed{Br\quad +K}OH\end{matrix}\right. = C_6H_2\left\{\begin{matrix}COOH\\OH\\OH\\OH\end{matrix}\right. +KBr.$$

Gallic acid is insoluble in cold water, but soluble in hot water, alcohol, and ether, and its solutions give first a precipitate and then form a dark-green solution with ferric chloride. A *blue-black ink* is made by adding gallic acid to a slightly acid solution of ferrous sulphate to which indigo carmine has also been added. When this dries on paper it oxidizes, giving a heavy black precipitate. When distilled gallic acid yields pyrogallic acid and carbon dioxide (see p. 267). **Airol** and **dermatol** are combinations of gallic acid with bismuth.

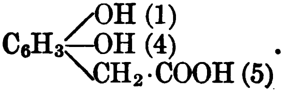
Tannic acid is much more soluble than gallic. It gives the same reaction with ferric chloride. It has a very extensive commercial use in tanning, in which process it forms insoluble and tough compounds with the proteid, etc., in skin. It is also employed, on account of its astringent properties, in medicine. Many derivatives of tannic acid have been prepared as substitutes for it, such as **tannalbin, tannacol, tannigen,** etc.

EXPERIMENTS. (1) Test solutions of gallic acid and tannic acid with ferric chloride.

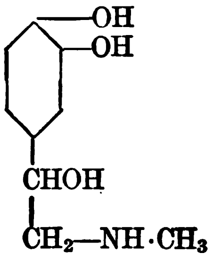
(2) Add tannic acid solution to some gelatin solution; the gelatin is precipitated.

(3) To a solution of quinine bisulphate (quinine dis-

solved in very dilute H_2SO_4) add tannic acid solution; the quinine is precipitated.

6. **Hydroxyl groups and fatty acid side chain.** **Tyrosin** is the chief representative. It is parahydroxyphenyl-α-aminopropionic acid, $C_6H_4\left\langle\begin{matrix}OH\\CH_2\cdot CHNH_2\cdot COOH\end{matrix}\right.$. Tyrosin is a decomposition product of proteid. It gives a test with Millon's reagent. Proteids which contain no tyrosin (as gelatin, certain albumoses, etc.) do not give this test. It occasionally occurs in the urine as characteristic crystals. **Phenylalanin** is closely related to tyrosin, differing only in not being a hydroxy-acid; its formula is $C_6H_5\cdot CH_2\cdot CHNH_2\cdot COOH$. **Homogentisic acid** has two hydroxyls; it is dihydroxyphenylacetic acid,  $C_6H_3\left\langle\begin{matrix}OH\ (1)\\OH\ (4)\\CH_2\cdot COOH\ (5)\end{matrix}\right.$. It has been found in the urine in cases of alcaptonuria.

Adrenalin. This is a derivative of pyrocatechol, for which the following structural formula has been suggested:[1]



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[1] Objections have been raised to this formula, so that it must still be considered an unsettled question.

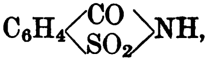
Adrenalin (also called *epinephrin*) is the active principle in the extract from the suprarenal capsule, and when its solution is injected into the circulation of an animal several important effects are observed, chief of which is rise of blood-pressure. A synthetic compound with the above formula can be prepared from pyrocatechol, and it produces the same physiological effects as adrenalin. It is, however, optically inactive, whereas adrenalin itself is optically active.

CHAPTER XXIX.

MIXED AROMATIC COMPOUNDS (*Continued*)
(ALSO INDICATORS AND DYES.)

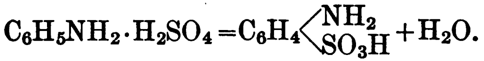
7. **Acid and nitro groups.** Benzoic acid readily reacts with nitric acid to form the nitrobenzoic acids. The meta variety is formed in greatest amount. As already pointed out, nitrobenzoic acids may also be obtained by oxidizing the corresponding nitrotoluenes (see p. 282).

8. **Acid and amino groups.** By reducing the nitro, benzoic acids with tin and hydrochloric acid (nascent hydrogen) amino derivatives of benzoic acid may be obtained (*cf.* reduction of nitrobenzene to aniline, p. 284). The ortho variety of these is known as *anthranilic acid*, $C_6H_4{<}\begin{matrix}COOH\\NH_2\ (o)\end{matrix}$. It is produced as an intermediate product in the preparation of aniline by boiling indigo with caustic alkali.

9. **Acid and sulpho groups.** Metasulphobenzoic acid is produced by the action of sulphuric acid on benzoic acid. The important substance **saccharin** is the imide of orthosulphobenzoic acid,  $C_6H_4{<}\begin{matrix}CO\\SO_2\end{matrix}{>}NH$, and is also called benzosulphinide. It is intensely sweet, and

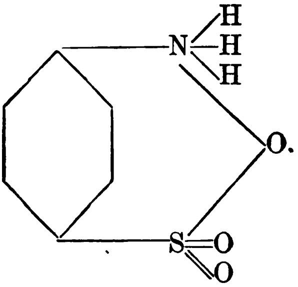
antiseptic; on account of these properties it is used as a medicine and a preservative.

10. **Sulphonic and amino groups.** By the action of sulphuric acid on aniline, aniline sulphate is first of all formed and then becomes converted into paraminobenzenesulphonic acid or **sulphanilic acid,** $C_6H_4{<}\genfrac{}{}{0pt}{}{NH_2}{SO_3H(p)}$, by dehydration:



$$C_6H_5NH_2 \cdot H_2SO_4 = C_6H_4{<}\genfrac{}{}{0pt}{}{NH_2}{SO_3H} + H_2O.$$

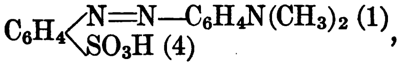
In sulphanilic acid it has been supposed that the amino and sulpho side chains are linked together through an oxygen atom so as to form an inner salt, thus:



Sulphanilic acid is soluble in hot water, but only sparingly so in cold water. Its solutions are acid in reaction, thus differing from taurin (aminoethyl-sulphonic acid, see p. 185). It is used in the manufacture of dyes, in a large number of which there exists the sulphonic acid group along with a diazo group. Two of these dyes, viz., **methyl orange** and **tropæolin OO,** are used as indicators in bio-chemistry.

EXPERIMENT. *Preparation of sulphanilic acid.* To 50 gm. of C.P. H_2SO_4 in a flask, add gradually 15 c.c. of aniline, and heat in an oil-bath at 180°–190° for about four hours, until a test-drop, diluted with water and treated with NaOH, shows no unchanged aniline. Cool, and pour into a beaker of cold water while stirring the latter. Filter off the crystals. Recrystallize from hot water.

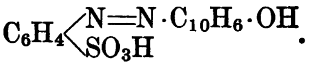
Helianthin is dimethyl-aminoazobenzene-sulphonic acid,



$$C_6H_4{<}\begin{matrix}N{=}N{-}C_6H_4N(CH_3)_2\ (1)\\ SO_3H\ (4)\end{matrix},$$

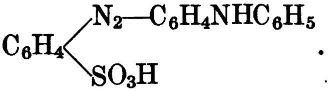
prepared by acting on benzene-diazonium-sulphonic acid with dimethylaniline. Its sodium salt is *methyl orange* (see indicators, p. 311).

Orange II is an azo dye, somewhat related to methyl orange in chemical structure:



$$C_6H_4{<}\begin{matrix}N{=}N\cdot C_{10}H_6\cdot OH\\ SO_3H\end{matrix}.$$

EXPERIMENT. Dissolve 10 gm. of dry sulphanilic acid in 100 c.c. of 2.5% Na_2CO_3 solution (made with anhydrous carbonate), and add 3.5 gm. of $NaNO_2$ dissolved in 20 c.c. of water. Cool with ice-water, gradually add diluted HCl (6 c.c. +10 c.c. H_2O), and finally add an acid solution of dimethylaniline (6 gm. + 6 c.c. HCl + 20 c.c. H_2O). Render the mixture alkaline with NaOH solution and add 20 gm. of NaCl. Filter off the methyl orange precipitate and crystallize from hot water. To a little dilute solution of methyl orange add some acid—a red colour is obtained. Save a sample of the crystals.

Tropæolin OO is diphenyl-aminoazobenzene-sulphonic acid,  $C_6H_4\begin{cases} N_2—C_6H_4NHC_6H_5 \\ SO_3H \end{cases}$. Its alcoholic solution gives a violet colour with free mineral acid; or, if its alcoholic solution be evaporated to dryness, the resulting residue, while still warm, gives a violet colour with free mineral acids. Applied in this latter manner the test is very delicate. It is thus used as an indicator in analysis of the gastric juice.

INDICATORS.

At this stage it will be convenient to discuss briefly the **theory of the action of indicators.**

These must possess weak acid or basic properties, and be, therefore, undissociated when in a free state, but dissociated when present as salts. In the dissociated state the anion must have a different colour from that of the undissociated compound.

Taking the three most commonly used indicators, phenolphthalein, methyl orange, and litmus, let us see in how far their actions can be thus explained.

(1) *Phenolphthalein.* This is of the nature of a very feeble acid, so that it is undissociated when in a free state, and when undissociated it is colourless. When dissociated, however, its anion has a red colour. Dissociation occurs when it is converted into a salt. Thus, when we titrate an acid with sodium hydroxide, using phenolphthalein as indicator, what happens is this: In the presence of the acid the phenolphthalein is undis-

sociated, and the solution is therefore colourless; as alkali is added the acid becomes gradually neutralized, until at last a trace of alkali in excess of that necessary to neutralize the acid is present; this trace combines with the phenolphthalein, forming a salt which then dissociates, so that the anion imparts its red colour to the solution.

The acid to be titrated must be distinctly stronger than phenolphthalein, for otherwise, before the former has all been neutralized, some of the salt formed will become hydrolyzed, and the base thus liberated will combine with the phenolphthalein and form a salt which, partially dissociating, will impart a pink tint to the solution. Thus, phenols cannot be titrated with phenolphthalein. On the other hand, such a feeble acid as carbonic is so much stronger than phenolphthalein that the latter can be employed as an indicator for titrating it. On this account carbon dioxide must be absent from the standard alkali used for titrating. Phenolphthalein can also be used for practically all organic fatty acids.

The base used for neutralization must also be a strong one. Thus, if a feeble base such as ammonia be employed, then the salt which it forms with the phenolphthalein will be so feeble that it will be decomposed by the water (hydrolysis), and the end reaction will be indefinite, an excess of ammonia requiring to be present before the decomposing effect of the water is overcome. Phenolphthalein must not, therefore, be used when ammonia or ammonium salts are present in a solution.

Phenolphthalein is the ideal indicator for weak acids, and should be employed along with a strong base.

(2) *Methyl Orange.* This is the sodium salt of a much stronger acid than phenolphthalein, and it dissociates readily in weak solution. When undissociated it is red, when dissociated its anion is yellow. Its dissociation in water is prevented by the presence of a trace of stronger acid,—such solutions are therefore red,—but if alkali be added in sufficient amount just to neutralize this acid, then the methyl orange partially dissociates and the solution becomes much paler, and if a trace more alkali be added still more dissociation occurs, so that the solution becomes bright yellow. Methyl orange is not affected by acid sodium phosphate (NaH_2PO_4), so that a weak acid such as this must be present in large excess before it can prevent the dissociation of methyl orange, therefore for titrating acid salts this indicator is unsuitable; for the same reasons it cannot be used for weak organic acids. On the other hand, it is suitable for practically all bases, since with all of them it will immediately form dissociable salts, which do not hydrolyze so long as any of the base is available (i.e., uncombined with the acid that is being titrated, which must, of course, be stronger than methyl orange).

Methyl orange is therefore especially useful for the titration of bases, including ammonia, and unsuitable for the weaker organic acids. The indicators used for the detection of mineral acid in the gastric contents belong to the same class as methyl orange, e.g., *Congo red* and *dimethylamidoazobenzene.*

While it is true that these indicators will not give an accurate titration value with organic acids, our experience (contrary to statements in clinical chemistry text-books) is that methyl orange, Congo red, and dimethylamidoazobenzene give a distinct colour reaction (as with mineral acids) even when used with very dilute organic acid solutions; for example, a $\frac{N}{286}$ lactic acid solution (1 drop of pure acid in 100 c.c. of water) reacts acid to these indicators. The phloroglucin-vanillin reagent, however, reacts only to mineral acid and can be used as the indicator when making a quantitative estimation of mineral acid in the presence of organic acids.

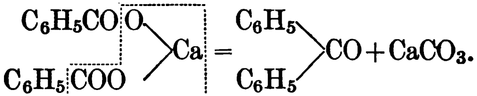
(3) *Litmus.* This stands between phenolphthalein and methyl orange in its properties. In the un-ionized state it is red, therefore red with acids; and in the ionized state blue, therefore blue with alkalies.

The importance to the student of thoroughly understanding the action of these three indicators will be evident from the fact that the blood and urine react very differently towards them. Towards methyl orange both blood and urine (even when the latter is acid to litmus) react alkaline or neutral, towards phenolphthalein they react acid, while towards litmus blood reacts alkaline and urine (usually) acid. The cause of this difference in action lies in the fact that in both of these animal fluids we have a mixture of NaH_2PO_4 and Na_2HPO_4. Occasionally these two salts are present in equivalent quantities in the urine (normally in milk also); in such a case the urine reacts acid to blue litmus and alkaline to red litmus (amphoteric reaction). This is due to the fact that NaH_2PO_4 is acid to litmus and Na_2HPO_4 is alkaline. In normal (acid) urine NaH_2PO_4 preponderates over the alkaline salt, therefore the urine reacts acid to litmus; in the blood, however, Na_2HPO_4 is present in excess, therefore it reacts alkaline to litmus. Both of these, even the acid-reacting NaH_2PO_4, are but feebly dissociated (i.e., furnish few ions) compared with the relatively strong acid in methyl orange; therefore they are unable to influence the degree of dissociation of methyl orange. Congo red acts in the same manner as methyl orange. Phenolphthalein, however, is so feeble an acid that both of these acid salts can readily keep it in the (practically) undissociated condition, and do not allow it to form its sodium salt, under which circumstances, as we have already stated, it remains colourless.

11. **Ketone group (CO) with two phenyl groups** (aromatic ketones), or linking together of a phenyl and fatty group (mixed aromatic fatty ketones).

These are prepared by methods analogous with those already studied in connection with aliphatic ketones, thus:

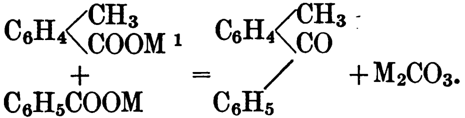
a. By distilling calcium benzoate, diphenyl ketone or *benzophenone* is produced:



$$\left.\begin{matrix}C_6H_5CO\,O\\C_6H_5\,COO\end{matrix}\right>Ca = \left.\begin{matrix}C_6H_5\\C_6H_5\end{matrix}\right>CO + CaCO_3.$$

(Benzophenone)

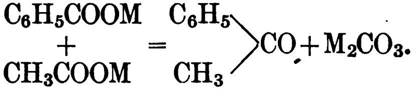
b. By distilling salts of two different aromatic acids, such as a salt of benzoic and one of toluic acid:



$$\begin{matrix}C_6H_4\left<\begin{matrix}CH_3\\COOM^{1}\end{matrix}\right.\\+\\C_6H_5COOM\end{matrix} = \begin{matrix}C_6H_4\left<\begin{matrix}CH_3\\CO\end{matrix}\right.\\ \diagup\\C_6H_5\end{matrix} + M_2CO_3.$$

(Phenyltolylketone)

c. By distilling a salt of an aromatic acid with one of a fatty acid:



$$\begin{matrix}C_6H_5COOM\\+\\CH_3COOM\end{matrix} = \left.\begin{matrix}C_6H_5\\CH_3\end{matrix}\right>CO + M_2CO_3.$$

(Methyl phenyl ketone or acetophenone)

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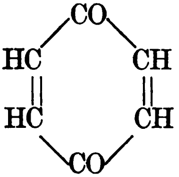
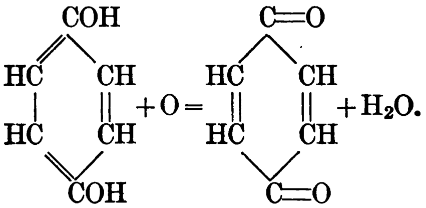
[1] The salt usually employed is that of calcium. M means a metal

Acetophenone may also be obtained by adding aluminium chloride to a mixture of benzene and acetyl chloride. It is a crystalline substance melting at 20.5°, and is slightly soluble in water. It is used in medicine as a hypnotic under the name of *hypnone*.

Quinones. These may be regarded as diketones.[1] The best known of them is **benzoquinone** or *quinone*, which has the structural formula , and may be prepared by oxidizing various para derivatives of benzene, but not ortho or meta derivatives. Thus *p*-phenolsulphonic acid, *p*-sulphanilic acid, *p*-amidophenol, etc., all yield quinone when oxidized. It is usually prepared, however, by oxidizing aniline with chromic acid or by oxidizing hydroquinol:



These reactions for its preparation (with the exception of its preparation from aniline) leave little doubt as to its structural formula.

The quinones are of a yellow colour and possess a pungent odour. They have oxidizing properties and are important in dye chemistry.

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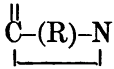
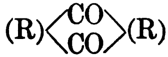
[1] These do not strictly belong to the class of bodies that we are considering as mixed compounds.

Several **dyes** have already been mentioned. All such bodies are supposed to owe their dyeing properties to the presence in them of a so-called *chromophore group*. Chromophore groups are of various kinds, of which the following are important:

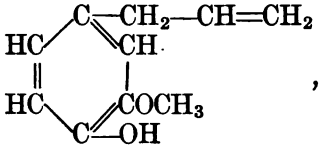
1. The azo group N═N, as in orange II (see p. 308).
2. The nitro group NO_2, as in picric acid (see p. 262).
3. The group  $\underbrace{\overset{\|}{C}-(R)-N}$, as in methyl violet (see p. 286).
4. The group  $(R)\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle(R)$, as in alizarin (see p. 321).

The presence in a substance of one of these groups alone is not, generally, sufficient to constitute it a dye; certain other groups, particularly OH and NH_2, must, as a rule, be attached to a chromophore-containing compound to render it available as a dye. These assisting or auxiliary groups are called *auxochromes*. The sulpho group is often introduced to render a dye soluble.

For many dyes a *mordant* is necessary, that is, an agent that will fix the colouring matter in the fibres of the fabric. For basic dyes tannic acid is largely used, while for acid dyes acetates of aluminium, chromium, and iron are commonly employed.

12. **Benzene derivatives having unsaturated carbon linkings in a side chain. Cinnamic aldehyde** has the formula $C_6H_5—CH═CH—CHO$. The corresponding acid is **cinnamic acid,** $C_6H_5 \cdot CH═CH \cdot COOH$. The aldehyde is the essential constituent of *cinnamon oil.* Synthetic cinnamic aldehyde is now displacing natural oil of cinnamon.

Cinnamic acid is a therapeutic agent. Other allyl derivatives of benzene are *eugenol* and *safrol*.

Eugenol, or parahydroxy-metamethoxy-allyl-benzene, , is the chief substance in *oil of cloves.*

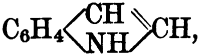
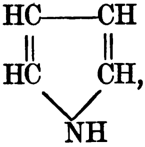
Eugenol acetamide, eugenol carbinol, eugenol iodide, and benzeugenol have been put on the market as medicinal preparations.

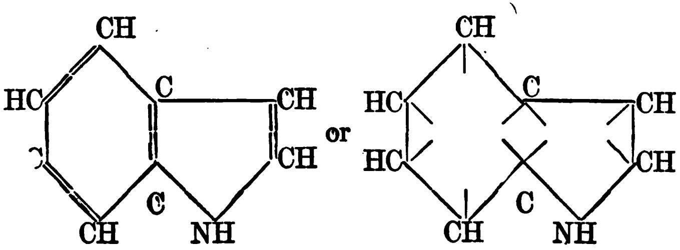
Safrol is contained in oil of sassafras and camphor oil. It is the methylene ether of allyl pyrocatechol, $C_6H_3 \cdot C_3H_5(OCH_2)(OH)$.

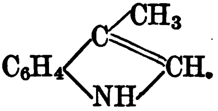
CHAPTER XXX.

AROMATIC COMPOUNDS HAVING CONDENSED RINGS.

PYRROL DERIVATIVES OF BENZENE.

Indol,  $C_6H_4\left<\begin{matrix}CH\\NH\end{matrix}\right>CH$, contains the pyrrol[1] nucleus,  condensed with the benzene nucleus, and may be represented thus:



Skatol is methyl indol,  $C_6H_4\left<\begin{matrix}C{-}CH_3\\NH\end{matrix}\right>CH$. Indol

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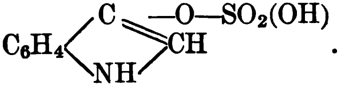
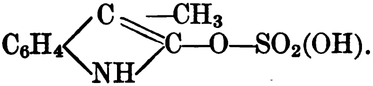
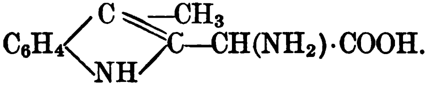
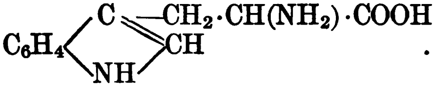
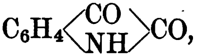
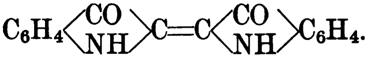
[1] The drug *iodol* is tetraiodopyrrol, $C_4I_4.NH$.

and skatol are contained in fæces, imparting the characteristic odour to the latter. They are produced in the intestine by the action of bacteria on the aromatic groups in proteid. They are volatile with steam.

Indican is the oxidation product of indol in combination with sulphuric acid as an ethereal sulphate, . It is indoxyl-sulphuric acid. It is sometimes present as a salt in the urine in considerable quantity. *Indigo* can be obtained from it, and occasionally indigo is deposited from urine containing much indican after ammoniacal decomposition sets in. To estimate the indican in the urine it is converted into indigo by various reagents, and this is then removed by shaking with chloroform. The blue chloroform solution can be compared with an indigo solution of known strength, and thus a colourimetric estimation may be made.

Skatoxyl-sulphuric acid is the corresponding derivative of skatol, . Another derivative of skatol is skatol-aminoacetic acid or **tryptophan,** . It has recently been claimed that tryptophan is indol-aminopropionic acid, . Like indol and skatol, it is a decomposition product of proteid, being produced during tryptic digestion. It gives a colour reaction with glyoxylic acid (see p. 172).

Directly related to indol is **isatin,**  $\mathrm{C_6H_4}{<}\begin{matrix}\mathrm{CO}\\ \mathrm{NH}\end{matrix}{>}\mathrm{CO}$, for the former can be obtained from the latter by reduction. **Indigo,** structurally, is a combination of two isatin molecules, the end oxygen atom of each molecule being eliminated, thus:

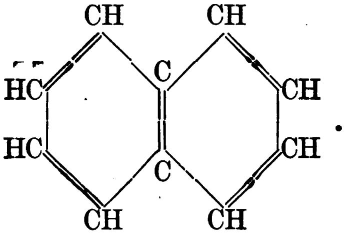


$$\mathrm{C_6H_4}{<}\begin{matrix}\mathrm{CO}\\ \mathrm{NH}\end{matrix}{>}\mathrm{C}=\mathrm{C}{<}\begin{matrix}\mathrm{CO}\\ \mathrm{NH}\end{matrix}{>}\mathrm{C_6H_4}.$$

Indigo can be produced from isatin. The synthesis of indigo on a commercial scale is one of the great achievements of chemistry. Most of the indigo marketed nowadays is artificially produced. Naphthalene is the starting-point of the synthesis. Indigo is a very valuable blue dye.

CONDENSED BENZENE RINGS.

Naphthalene ($C_{10}H_8$) contains two benzene rings connected together in the following manner:

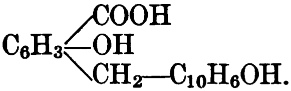


It forms white crystals melting at 79.6° and having a tar-like odour. It is volatile and is contained in coal-gas, being also a constituent of the distillate from coal-tar.

Experiments. (1) Heat some naphthalene in a dry test-tube. It sublimes.

(2) Try Friedel and Crafts' reaction with some naphthalene dissolved in chloroform (see p. 253).

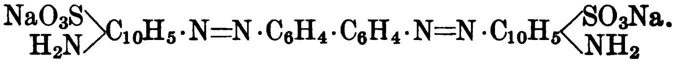
The **naphthols,** $C_{10}H_7\cdot OH$, correspond to phenols. Alpha-naphthol (melting-point 95°) and beta-naphthol (melting-point 122°) are both of importance. **Epicarin** is related to naphthol; its formula is



$$C_6H_3\left<\begin{matrix}COOH\\OH\\CH_2—C_{10}H_6OH.\end{matrix}\right.$$

Orphol is a combination of beta-naphthol with bismuth nitrate. All these substances are antiseptics. *Alpha- and beta-naphthylamines,* $C_{10}H_7\cdot NH_2$, are used as reagents.

Congo red is a complex diazonium derivative of naphthylamine-sulphonic acid. Its formula is

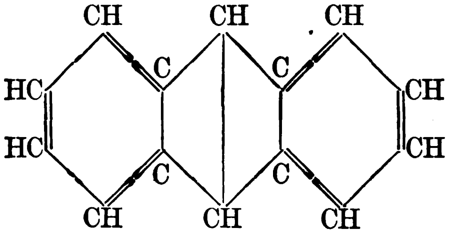


$$\left.\begin{matrix}NaO_3S\\H_2N\end{matrix}\right>C_{10}H_5\cdot N{=}N\cdot C_6H_4\cdot C_6H_4\cdot N{=}N\cdot C_{10}H_5\left<\begin{matrix}SO_3Na.\\NH_2\end{matrix}\right.$$

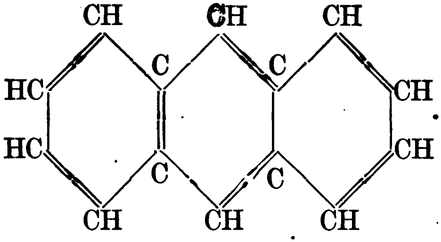
Its colour becomes blue in the presence of free acids.

Santonin, $C_{15}H_{18}O_3$, is a derivative of naphthalene and is the anhydride or lactone of santoninic acid.

Anthracene, $C_{14}H_{10}$, is a hydrocarbon containing three benzene rings condensed together:

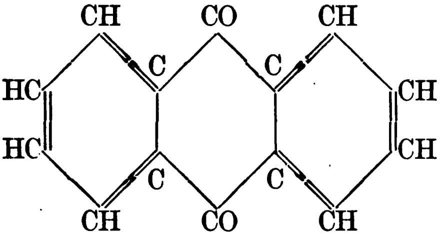


or



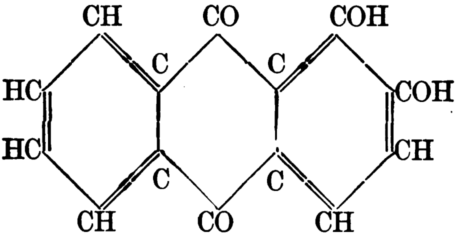
It occurs in coal-tar in small quantity and is used in manufacturing alizarin. Its crystals melt at 216.5° (corrected).

One of the important derivatives of anthracene is **anthraquinone,**

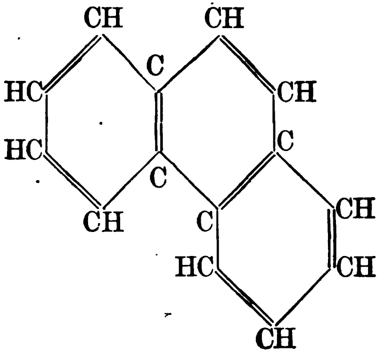


$, C_{14}H_8O_2.$

Dihydroxyanthraquinone is the very important dye **alizarin,** $C_{14}H_6O_2(OH)_2$:

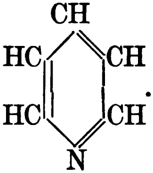


Chrysophanic acid, $C_{14}H_5O_2(CH_3)(OH)_2$, and **chrysarobin,** $C_{30}H_{26}O_7$, are anthracene derivatives of therapeutic importance. Isomeric with anthracene is **phenanthrene,** $C_{14}H_{10}$:



CHAPTER XXXI.

AROMATIC BASES CONTAINING NITROGEN IN THE NUCLEUS.

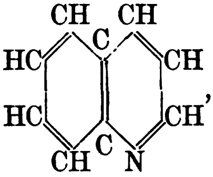
Pyridine Bases. These are ammonia derivatives and of great importance on account of their relationship to certain alkaloids which will be discussed presently. The simplest member of the series is pyridine, which has the structural formula . It may therefore be considered as benzene with a CH group replaced by nitrogen (C_5H_5N). There are several methyl pyridines.

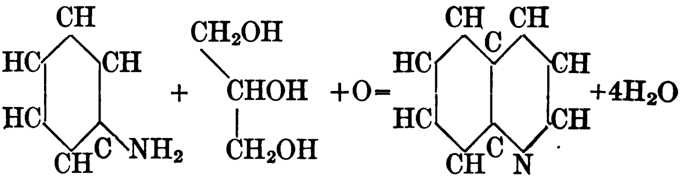
The pyridines are contained in coal-tar, and are formed when bones are distilled, being produced by the action on one another at high temperatures of acrolein, ammonia, methylamine, etc.

Pyridine is a colourless liquid with an odour like tobacco-smoke. It boils at 115° C. It mixes readily with water, the resulting solution being strongly alkaline. Like other tertiary ammonia bases, it directly combines with acids to form crystalline salts. When warmed with alkyl halides addition products are formed, and if these be treated with caustic potash a very pungent and disagreeable odour is evolved.

EXPERIMENTS. (1) Dissolve some pyridine in water; test alkalinity with litmus. Notice the odour.

(2) Then neutralize the solution with HCl, add a few drops of platinic chloride solution, and boil; a yellow precipitate of $(C_5H_5N)_2PtCl_4$ forms.

Quinoline is another tertiary ammonia base. It may be considered as naphthalene in which a CH group has been replaced by N: , C_9H_7N. It is found in coal-tar. When certain alkaloids, particularly quinine and cinchonine, are distilled with potassium hydroxide, quinoline is obtained. Quinoline can be synthesized from aniline and glycerol in the presence of nitrobenzene and concentrated sulphuric acid (see exp. below):



(Aniline) (Glycerol) (Quinoline)

Quinoline is a liquid boiling at 237°. By proper treatment of quinoline, pyridine can be derived from it. Many alkaloids are quinoline derivatives.

EXPERIMENT. *Synthesize quinoline.* In a litre flask mix 15 gm. of nitrobenzene, 24 gm. of aniline, and 75 gm. of glycerol; add 62 gm. of C.P. H_2SO_4 while agitating the mixture. Connect with an air-condenser having a diameter of 2 cm., and heat the flask very gradually on a sand bath. Wrap the condenser with a damp rag. When the reaction begins (sudden bubbling) remove the flame. If the action is very vigorous, cool the upper part of the flask with an air stream from a bellows. When the mixture becomes quiet, heat for three hours on a sand bath. Then dilute with 300 c.c. of water and distil with steam. When no more oily drops of nitrobenzene come over, stop the distilling. Cool partially, render the mixture alkaline with strong NaOH solution, and again distil with steam, thus removing the quinoline and aniline. This last distillate is specially treated to convert the aniline into phenol, as was directed in the experiment under phenol (see p. 259). Diazotize the cooled liquid after rendering it distinctly acid with dilute H_2SO_4, warm in a bath, make alkaline (the phenol becomes fixed as a phenolate, while quinoline is set free), and distil with steam. Extract the quinoline from the distillate with ether and proceed just as was done with phenol.

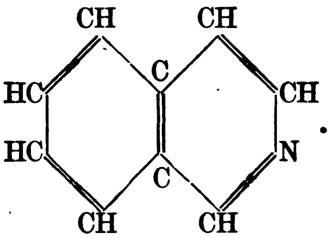
Thalline, $C_9H_9(OCH_3)NH$, and

Kairine, $C_9H_9(OH)N—C_2H_5$, are quinoline derivatives that have been used as antipyretics.

Analgen (quinalgen) is a more recent antipyretic, $C_9H_5(OC_2H_5)NH(COC_6H_5)N$.

Kynurenic acid, occurring in the urine of dogs, is a quinoline derivative, $C_9H_5N(OH)(COOH)$.

Isoquinoline, C_9H_7N, is an isomer of quinoline:



It is of importance because of the derivation of many alkaloids from it.

SYNOPSIS.

Aromatic Compounds.

A. BENZENE HYDROCARBONS.
- Benzene derivatives.
  - 1. *Halogen derivatives.*
  - 2. *Hydroxy derivatives.*
    - a. Phenols
      - Ethers.
      - Ethereal salts.
      - (1) Monacid phenols
        - Substitution products.
      - (2) Diacid phenols.
      - (3) Triacid phenols.
      - (4) Hexacid phenol derivative.
    - b. Fatty alcohol side-chain compounds and derivatives
      - Alcohols (primary).
      - Aldehydes.
      - Monobasic acids
        - Salts.
        - Ethereal salts.
  - 3. *Dibasic acids.*

4. *Nitrogen derivatives.*
    - (*a*) Nitro compounds.
    - (*b*) Amino compounds.
    - (*c*) Diazo compounds.
5. *Sulphur derivatives.*
6. *Mixed compounds.*
    - (1) Phenol and sulphonic groups.
    - (2) Phenol and nitro groups.
    - (3) Phenol and amino groups.
    - (4) Phenol and primary alcohol groups.
    - (5) Hydroxy-acids.
    - (6) Hydroxyl groups and fatty acid side chain.
    - (7) Acid and nitro groups.
    - (8) Acid and amino groups.
    - (9) Acid and sulpho groups.
    - (10) Sulphonic and amino groups.
    - (11) Ketone linkings and quinones.
    - (12) Unsaturated side-chain combinations with benzene derivatives.

B. PYRROL DERIVATIVES OF BENZENE.

C. CONDENSED BENZENE RINGS.

1. *Naphthalene.*
2. *Anthracene.*
3. *Phenanthrene.*

D. AROMATIC BASES HAVING NITROGEN IN THE NUCLEUS.

1. *Pyridine bases.*
2. *Quinoline bases.*
3. *Isoquinoline bases.*
4. *Alkaloids.*

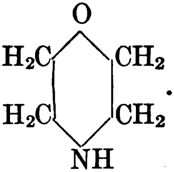
CHAPTER XXXII.

ALKALOIDS AND DRUG PRINCIPLES.

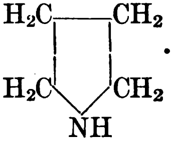
ALKALOIDS.

In its broadest application the term alkaloid includes all nitrogenous organic substances that are basic in character (*alkaloid = alkali-like*). Caffeine and theobromine, purin bases and other leucomaines, choline, muscarine, and other ptomaines are all called alkaloids.

In this chapter we intend to consider only those alkaloids which are secondary or tertiary ammonia bases, containing one or more aromatic nuclei. Those whose structure is known are derivatives of pyridine, pyrrolidine, quinoline, isoquinoline, or morpholine. *Morpholine* has the formula



Pyrrolidine is derived from pyrrol (see p. 317); it is



The empirical formulæ of the chief alkaloids are as follows:

Coniine.	$C_8H_{17}N$.	
Nicotine.	$C_{10}H_{14}N_2$.	
Sparteine.	$C_{15}H_{26}N_2$.	
Hydrastinine.	$C_{11}H_{11}NO_2$.	
Pilocarpine.	$C_{11}H_{16}N_2O_2$.	
Emetine.	$C_{15}H_{21}NO_2$.	
Physostigmine.	$C_{15}H_{21}N_3O_2$	(Eserine).
Eseridine	$C_{15}H_{23}N_3O_3$.	
Homatropine.	$C_{16}H_{21}NO_3$.	
Lobeline.	$C_{16}H_{24}NO$.	
Apomorphine.	$C_{17}H_{17}NO_2$.	
Morphine.	$C_{17}H_{19}NO_3$.	
Cocaine.	$C_{17}H_{21}NO_4$.	
Hyoscine.	$C_{17}H_{21}NO_4$	(Scopolamine).
Atropine.	$C_{17}H_{23}NO_3$	Isomers.
Hyoscyamine.	$C_{17}H_{23}NO_3$	
Codeine.	$C_{18}H_{21}NO_3$.	
Thebaine.	$C_{19}H_{21}NO_3$.	
Cinchonine.	$C_{19}H_{22}N_2O$	Isomers.
Cinchonidine.	$C_{19}H_{22}N_2O$	
Berberine.	$C_{20}H_{17}NO_4$.	
Papaverine.	$C_{20}H_{21}NO_4$.	
Quinine.	$C_{20}H_{24}N_2O_2$	(Isomer, Quinidine)
Hydrastine.	$C_{21}H_{21}NO_6$.	
Strychnine.	$C_{21}H_{22}N_2O_2$.	
Narcotine.	$C_{22}H_{23}NO_7$.	
Colchicine.	$C_{22}H_{25}NO_6$.	
Gelseminine.	$C_{22}H_{26}N_2O_3$.	
Yohimbine.	$C_{22}H_{28}N_2O_3$.	
Brucine.	$C_{23}H_{26}NO_3$.	

Narceine	$C_{23}H_{27}NO_8$.
Jervine	$C_{26}H_{37}NO_3$.
Veratrine	$C_{32}H_{49}NO_9$.
Aconitine	$C_{33}H_{45}NO_{12}$.

Coniine and nicotine are the only important alkaloids that contain no oxygen and that are volatile liquids. Sparteine is a liquid, but non-volatile. All of the alkaloids form salts with acids; these salts are very much more soluble in water and alcohol than the free alkaloids. The free alkaloids, on the other hand, are more soluble than their salts in the immiscible solvents—ether, chloroform, benzene, and amyl alcohol.

All alkaloids are precipitated by phosphomolybdic and phosphotungstic acids, most of them by potassium mercuric iodide and many of them by tannic acid.

Most of the alkaloids are optically active, generally lævorotatory.

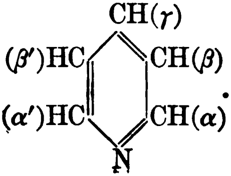
Many of the alkaloids are extremely poisonous, but in minute doses they are very valuable remedies.

The alkaloids here considered are of vegetable origin, practically all coming from dicotyledonous plants.

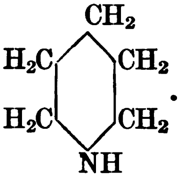
We shall consider now some of the facts that are known in regard to the structure of alkaloids.

PYRIDINE DERIVATIVES.

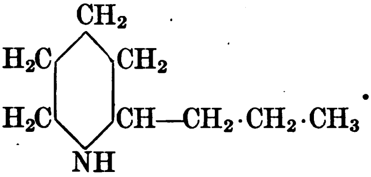
It is necessary to designate the positions of groups in the pyridine ring thus:



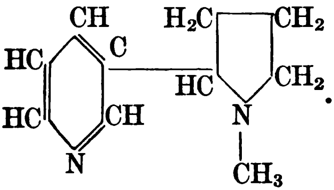
Piperidine is the simplest derivative,



Coniine is α-propyl piperidine,



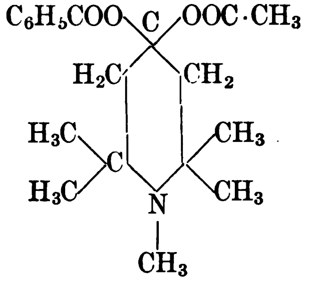
Nicotine is a pyrrol derivative (see p. 317) of pyridine, the attachment of the pyrrol ring to pyridine being in the β position (pyridyl-β-tetrahydromethyl pyrrol):



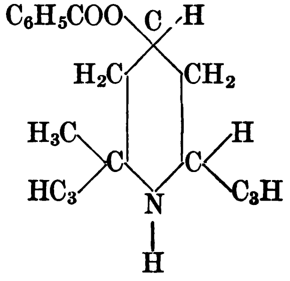
Coniine and nicotine have marked similarities; both are volatile liquids having a strong odour, and both are very poisonous. Coniine is obtained from hemlock-seed, and nicotine from tobacco. Both are strongly alkaline to litmus. Synthetic α-propyl piperidine is identical with coniine, except that it is optically inactive. Optically active coniine can be obtained from this by securing crystals of the tartrate of coniine, the first crop of crystals containing only dextroconiine. This was the first synthesis (1886) of a natural alkaloid.

Pilocarpine has been considered a pyridine derivative, but this is disputed.

The artificial alkaloids α- and β- **eucaine** are complex piperidine bodies. **Euphthalmine** is a derivative of β-eucaine.



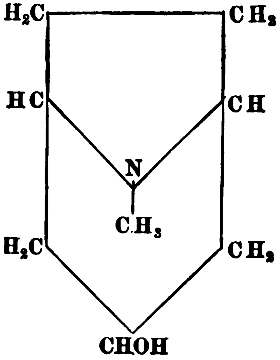
(α-eucaine)



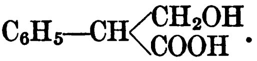
(β-eucaine)

PYRROLIDINE DERIVATIVES.

The alkaloids of the cocaine and atropine group are all pyrrolidine derivatives. This class of alkaloids is of great pharmacological importance. Cocaine is an invaluable local anæsthetic, while members of the atropine group are used to dilate the pupil. The basal substance for all of these compounds is tropine. This has, as will be noticed, a secondary closed carbon chain:

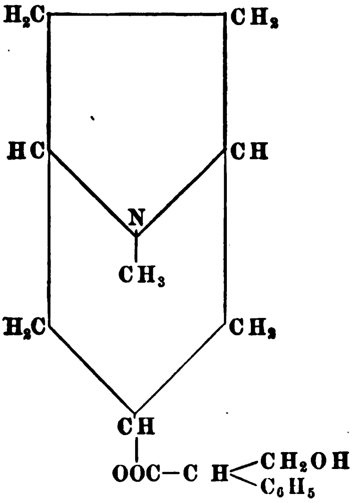


Tropic acid has the formula



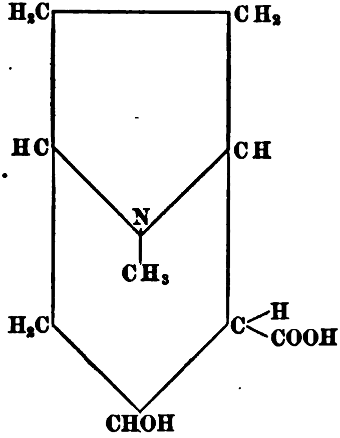
$$C_6H_5{-}CH\left\langle\begin{array}{l}CH_2OH\\COOH\end{array}\right. .$$

Atropine is the tropine ester (tropine being an alcohol) of tropic acid, its formula being

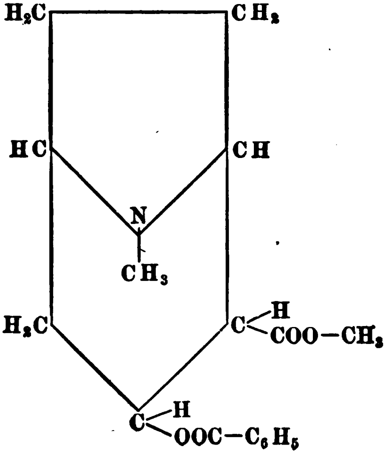


Atropine and its isomers have the same pharmacological action.

If in tropine an H atom of a CH_2 group of the secondary ring be replaced by COOH, ecgonine is obtained:



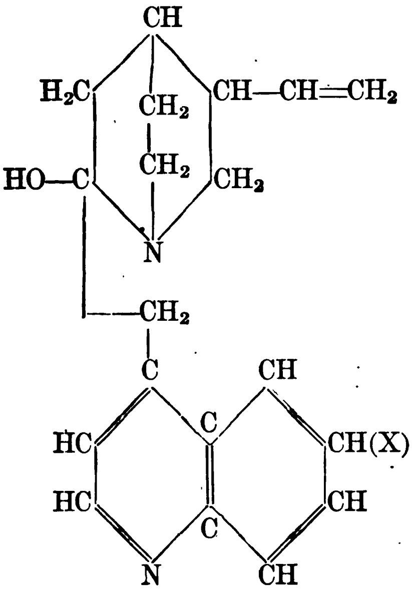
From this is derived **cocaine,** which is the methyl ester of benzoyl ecgonine:



Besides this similarity of cocaine to atropine in chemical structure, there are marked resemblances in pharmacological action.

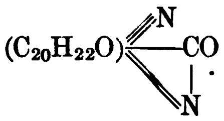
QUINOLINE DERIVATIVES.

The chief alkaloids of this class are the cinchona alkaloids. The following formula has been suggested for **cinchonine:**

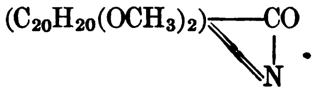


Quinine has the same formula, except that an H atom at the position marked (X) is replaced by the methoxy group (OCH_3).

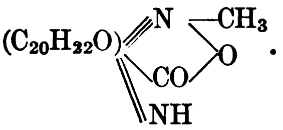
Strychnine and brucine are believed to be quinoline derivatives, but their structure has not been fully worked out. The nature of the nitrogen linkings is known. **Strychnine** may be represented as



Brucine differs from it in having two methoxy (OCH_3) groups in the place of two hydrogen atoms and in dropping out ON:



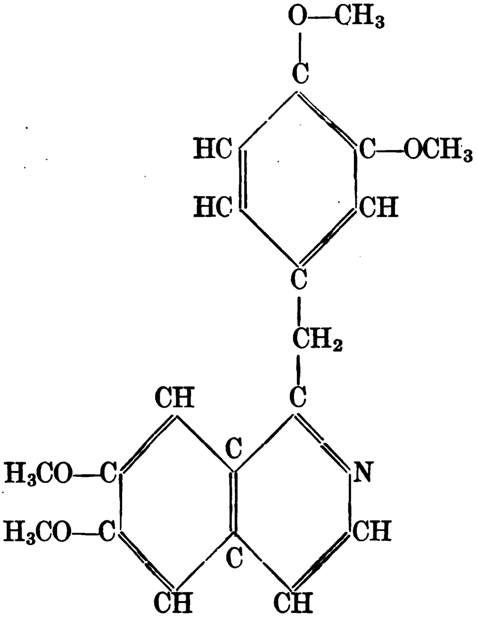
Methyl strychnine is obtained as follows: strychnine is treated with methyl iodide; an addition compound is formed, $C_{21}H_{22}N_2O_2 \cdot ICH_3$, the N atom which has the triple bond changing its valence from III to V in order to attach the I and CH_3; when this is treated with silver sulphate and barium hydroxide solution the product is the ammonium base, $C_{21}H_{22}N_2O_2 \cdot CH_3(OH)$; on standing this becomes methyl strychnine,



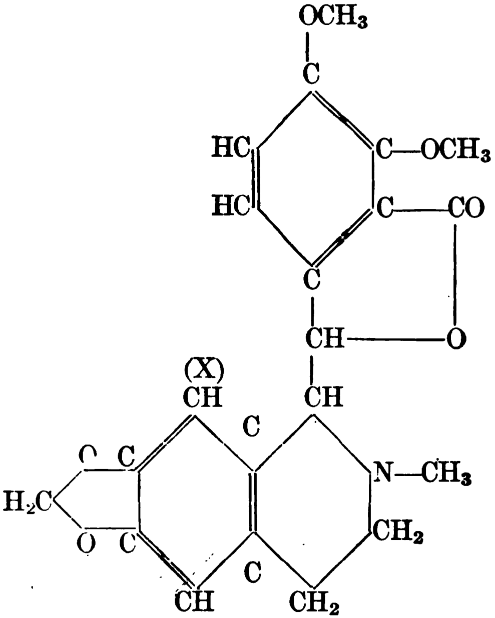
Dimethyl strychnine has the same formula, except that CH_3 is substituted for H in the NH group. This is produced from methyl strychnine in exactly the same manner as the latter is derived from strychnine; in this case, however, no oxygen is introduced into the molecule, but only CH_3.

ISOQUINOLINE DERIVATIVES.

The *minor opium alkaloids*, papaverine, narcotine, and narceine, also *hydrastine* and *berberine*, belong to this group. These alkaloids are of very little importance (except hydrastine) therapeutically. **Papaverine** has the simplest structure; it is tetramethoxybenzylisoquinoline; its formula is



Hydrastine has a similar but more complicated structure:



Narcotine is methoxyhydrastine, the OCH_3 group **taking the place of H at (X).**

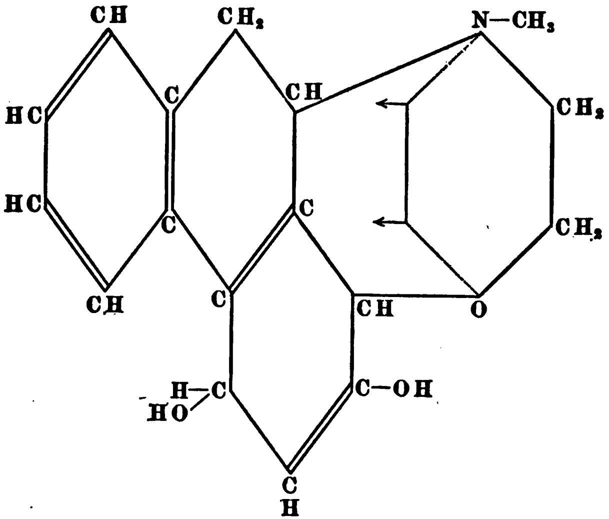
Hydrastinine is an alkaloid prepared by oxidation of hydrastine with nitric acid. It has a much stronger physiological action than hydrastine.

MORPHOLINE DERIVATIVES.

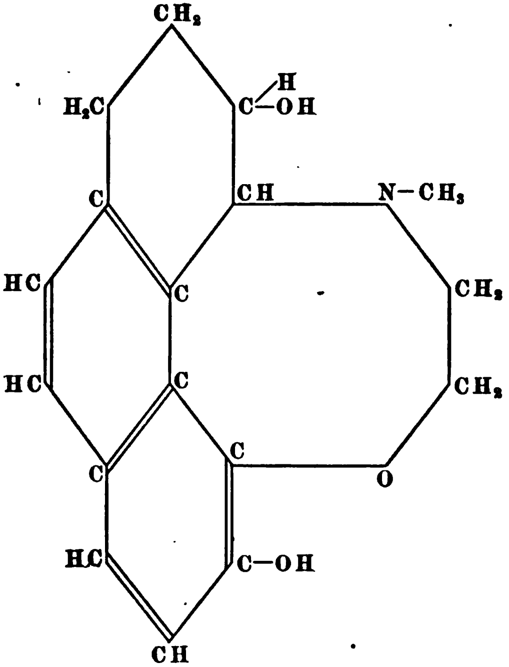
These are *morphine*, *codeine*, and *thebaine*, all of them being alkaloids present in opium. Derivatives of morphine artificially produced are apomorphine, dionine, heroine and peronine.

Morphine is the most valuable alkaloid for therapeutic purposes that we have. Its derivatives are much weaker in physiological action.

Methyl morpholine condensed with dihydroxyphenanthrene is supposed to make up the morphine molecule:



There is a difference of opinion as to where the two hydroxyls should be attached. The following formula has been proposed recently:



Codeine has the above formula, with CH_3 substituted for the H of one OH group. Thus codeine is the monomethyl ether of morphine. Codeine has been prepared from morphine by treating the latter with methyl iodide in the presence of caustic potash (see exp. below):

$$\underset{\text{(Morphine)}}{C_{17}H_{17}NO(OH)_2}+CH_3I+KOH=\underset{\text{(Codeine)}}{C_{17}H_{17}NO(OH)(OCH_3)}$$
$$+KI+H_2O.$$

Thebaine has two less hydrogen atoms attached to the phenanthrene nucleus, and has two OCH_3 groups in place of the two hydroxyls of morphine.

By the action of concentrated mineral acids, a molecule of water can be removed from morphine, producing **apomorphine:**

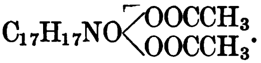
$$\underset{\text{(Morphine)}}{C_{17}H_{19}NO_3} - H_2O = \underset{\text{(Apomorphine)}}{C_{17}H_{17}NO_2}.$$

It is supposed that in apomorphine the phenanthrene nucleus is condensed with quinoline instead of with morpholine.

Other derivatives of morphine have been recently put forward as therapeutic agents.

Dionine is the hydrochloride of the ethyl ether of morphine, $C_{17}H_{17}NO(OH)(OC_2H_5) \cdot HCl$.

Heroine is diacetylmorphine,



$$C_{17}H_{17}NO\begin{cases}OOCCH_3\\OOCCH_3\end{cases}.$$

Peronine is the hydrochloride of the benzyl ether of morphine,

$$C_{17}H_{17}NO(OH)(OCH_2C_6H_5) \cdot HCl.$$

EXPERIMENTS. (1) Test solutions of morphine sulphate and quinine sulphate with alkaloidal reagents, as phosphomolybdic acid, mercuric potassium iodide, and tannic acid solutions.

(2) *Produce codeine.* Dissolve 1 gm. of morphine (pure alkaloid) in 30 c.c. of pure methyl alcohol, attach a wide vertical air-condenser tube, through this tube drop pieces of clean metallic sodium the size of a bean, after one piece becomes dissolved drop in another, and so on until the alcohol will dissolve no more sodium,

meanwhile keeping the flask cool. To this sodium methylate-morphine mixture add 10 gm. of methyl iodide and heat in a water bath at 90° for two to three hours, using a reflux condenser. Add 20 c.c. of water and distil off all volatile materials on a boiling water bath. Cool, transfer to a separating funnel, and shake with several portions of benzene. Dry the combined benzene extracts with calcium chloride, filter into an evaporating dish, and evaporate to dryness on a water bath. Dissolve some of the residue with 2% HCl, warming gently.

Test a drop of the solution with potassium mercuric iodide solution. Also make the following tests: (*a*) make a paste of some ammonium molybdate with a few drops of C.P. H_2SO_4, add a drop of the alkaloid solution—a blue colour is obtained; (*b*) to a few drops of the solution add 2 c.c. of H_2SO_4 containing 1 drop of formaline—a reddish-violet colour. These two tests are given also by morphine, but morphine cannot be extracted by means of benzene. A test given by codeine, but not by morphine, is this: to the residue in the evaporating dish add about 1 c.c. of 20% H_2SO_4 and warm—a faint pink colour appears.

DRUG PRINCIPLES OF UNKNOWN STRUCTURE.

Cantharidin, $C_{10}H_{12}O_4$, is a benzene derivative.

Picrotoxin is $C_{30}H_{34}O_{13}$ (or $C_{45}H_{50}O_{19}$).

Aloin has the formula $C_{16}H_{16}O_7$.

APPENDIX.

Note to the Instructor.[1] If it is desired to shorten the time given to the experiments, we would advise omitting the following: preparation of phenol from potassium benzene sulphonate (see p. 294), preparation of hippuric acid from urine (see p. 278), the diazonium experiments (see p. 289). preparation of sulphanilic acid (see p. 307), of quinoline (see p. 325), and of codeine (see p. 341).

Diazonium salt may be prepared as a demonstration by the instructor.

To permit of using one apparatus (as a Beckmann apparatus or a combustion furnace) with the entire class, we would suggest dividing the class or a section of it into five groups of three or four men each, the men of each group working together on a particular experiment, but the various groups performing different experiments on the same day. For example, one group may do crystallization and melting-point experiments (see pp. 9, 10), a second may carry out fractional distillation (see p. 12) and boiling-point determination (see p. 16), a third may make specific gravity determinations (see p. 19), a fourth may do a combustion analysis (see p. 26), and a fifth may use the Beckmann apparatus (see p. 49). Each group will, of course, have to take the experiments in a different order, thus:

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[1] We can recommend as valuable books for reference the text-books of organic chemistry by Remsen, Holleman, W. A. Noyes. Bernthsen, and Meyer and Jacobson, the laboratory manuals by Gattermann (translated by Schober) and Cohen, and "Introduction to Physical Chemistry," by Walker.

Group	I,	Lessons	1, 2, 3, 4, 5.
"	II,	"	2, 3, 4, 5, 1.
"	III,	"	3, 4, 5, 1, 2.
"	IV,	"	4, 5, 1, 2, 3.
"	V,	"	5, 1, 2, 3, 4.

Spellings. We have retained the ending "ine" in the case of amines and alkaloids, with the idea of indicating by this means the organic substances that are *distinctly basic* in character.

Formulæ. We strongly advise that the learning of empirical formulæ by the student be discouraged, but that, on the other hand, the student be thoroughly drilled in giving structural formulæ.

REFERENCE TABLES.

TABLE I.

Specific Gravity and Percentage of Alcohol.

[According to Squibb.]

Per Cent Alcohol by Volume.	Per Cent Alcohol by Weight.	Specific Gravity.	
		At $\frac{15.56°}{15.56}$C.	At $\frac{25°}{15.56}$C.
1	0.79	0.9985	0.9970
2	1.59	.9970	.9953
3	2.39	.9956	.9938
4	3.20	.9942	.9922
5	4.00	.9930	.9909
6	4.80	.9914	.9893
7	5.61	.9898	.9876
8	6.42	.9890	.9868
9	7.23	.9878	.9855
10	8.04	.9869	.9846
11	8.86	.9855	.9831
12	9.67	.9841	.9816
13	10.49	.9828	.9801
14	11.31	.9821	.9793
15	12.13	.9815	.9787
16	12.95	.9802	.9773
17	13.78	.9789	.9759
18	14.60	.9778	.9746
19	15.43	.9766	.9733
20	16.26	.9760	.9726
21	17.09	.9753	.9719
22	17.92	.9741	.9706
23	18.76	.9728	.9692
24	19.59	.9716	.9678
25	20.43	.9709	.9668
26	21.27	.9698	.9655
27	22.11	.9691	.9646
28	22.96	.9678	.9631
29	23.81	.9665	.9617
30	24.66	.9652	.9603
31	25.51	0.9643	0.9594
32	26.37	.9631	.9582
33	27.23	.9618	.9567
34	28.09	.9609	.9556
35	28.96	.9593	.9538
36	29.83	.9578	.9521
37	30.70	.9565	.9507
38	31.58	.9550	.9489
39	32.46	.9535	.9473
40	33.35	.9519	.9456
41	34.24	.9503	.9438
42	35.13	.9490	.9424
43	36.03	.9470	.9402
44	36.93	.9452	.9382
45	37.84	.9434	.9363
46	38.75	.9416	.9343
47	39.67	.9396	.9323
48	40.60	.9381	.9307
49	41.52	.9362	.9288
50	42.52	.9343	.9267
51	43.47	.9323	.9246
52	44.42	.9303	.9226
53	45.36	.9283	.9205
54	46.32	.9262	.9184
55	47.29	.9242	.9164
56	48.26	.9221	.9143
57	49.23	.9200	.9122
58	50.21	.9178	.9100
59	51.20	.9160	.9081
60	52.20	.9135	.9056

TABLE I—*Continued*

[According to Squibb.]

Per Cent Alcohol by Volume.	Per Cent Alcohol by Weight.	Specific Gravity.		Per Cent Alcohol by Volume.	Per Cent Alcohol by Weight.	Specific Gravity.	
		At $\frac{15.56^\circ}{15.56}$C.	At $\frac{25^\circ}{15.56}$C.			At $\frac{15.56^\circ}{15.56}$C.	At $\frac{25^\circ}{15.56}$C.
61	53.20	0.9113	0.9034	81	74.74	0.8611	0.8530
62	54.21	.9090	.9011	82	75.91	.8581	.8500
63	55.21	.9069	.8989	83	77.09	.8557	.8476
64	56.22	.9047	.8969	84	78.29	.8526	.8444
65	57.20	.9025	.8947	85	79.50	.8496	.8414
66	58.27	.9001	.8923	86	80.71	.8466	.8384
67	59.32	.8973	.8895	87	81.94	.8434	.8352
68	60.38	.8949	.8870	88	83.19	.8408	.8326
69	61.42	.8925	.8846	89	84.46	.8373	.8291
70	62.50	.8900	.8821	90	85.75	.8340	.8258
71	63.58	.8875	.8796	91	87.00	.8305	.8223
72	64.66	.8850	.8771	92	88.37	.8272	.8191
73	65.74	.8825	.8746	93	89.71	.8237	.8156
74	66.83	.8799	.8719	94	91.07	.8199	.8118
75	67.93	.8769	.8689	95	92.46	.8164	.8083
76	69.05	.8745	.8665	96	93.89	.8125	.8044
77	70.18	.8721	.8641	97	95.34	.8084	.8003
78	71.31	.8696	.8616	98	96.84	.8041	.7960
79	72.45	.8664	.8583	99	98.39	.7995	.7914
80	73.59	.8639	.8558	100	100.00	.7946	.7865

TABLE II.

WEIGHT IN MILLIGRAMS OF 1 C.C. OF MOIST NITROGEN AT VARIOUS TEMPERATURES AND UNDER VARIOUS PRESSURES (MILLIMETRES OF MERCURY).

Temperature.	728	730	732	734	736	738	740	742
10°	1.1466	1.1498	1.1529	1.1561	1.1593	1.1625	1.1657	1.1689
11°	1.1415	1.1447	1.1479	1.1511	1.1542	1.1574	1.1606	1.1638
12°	1.1364	1.1396	1.1428	1.1459	1.1491	1.1523	1.1554	1.1586
13°	1.1314	1.1345	1.1377	1.1409	1.1440	1.1472	1.1503	1.1535
14°	1.1263	1.1294	1.1326	1.1357	1.1389	1.1420	1.1452	1.1483
15°	1.1211	1.1243	1.1274	1.1305	1.1337	1.1368	1.1399	1.1431
16°	1.1160	1.1191	1.1222	1.1253	1.1285	1.1316	1.1347	1.1378
17°	1.1107	1.1138	1.1170	1.1201	1.1232	1.1263	1.1294	1.1325
18°	1.1054	1.1085	1.1117	1.1148	1.1179	1.1209	1.1241	1.1272
19°	1.1001	1.1032	1.1063	1.1094	1.1125	1.1156	1.1187	1.1218
20°	1.0948	1.0979	1.1009	1.1040	1.1071	1.1102	1.1133	1.1164
21°	1.0894	1.0924	1.0955	1.0986	1.1017	1.1047	1.1078	1.1109
22°	1.0839	1.0870	1.0900	1.0931	1.0961	1.0992	1.1023	1.1053
23°	1.0784	1.0814	1.0845	1.0875	1.0906	1.0936	1.0967	1.0997
24°	1.0728	1.0758	1.0789	1.0819	1.0849	1.0880	1.0910	1.0940
25°	1.0671	1.0701	1.0732	1.0762	1.0792	1.0823	1.0853	1.0883

Temp.	744	746	748	750	752	754	756	758
10°	1.1721	1.1753	1.1785	1.1817	1.1848	1.1880	1.1912	1.1944
11°	1.1670	1.1701	1.1733	1.1765	1.1797	1.1829	1.1860	1.1892
12°	1.1618	1.1649	1.1681	1.1713	1.1744	1.1776	1.1808	1.1839
13°	1.1566	1.1598	1.1630	1.1661	1.1693	1.1724	1.1756	1.1787
14°	1.1515	1.1546	1.1577	1.1609	1.1640	1.1672	1.1703	1.1735
15°	1.1462	1.1493	1.1525	1.1556	1.1587	1.1619	1.1650	1.1681
16°	1.1409	1.1441	1.1472	1.1503	1.1534	1.1566	1.1597	1.1628
17°	1.1356	1.1387	1.1419	1.1450	1.1481	1.1512	1.1543	1.1574
18°	1.1303	1.1334	1.1365	1.1396	1.1427	1.1458	1.1489	1.1520
19°	1.1248	1.1279	1.1310	1.1341	1.1372	1.1403	1.1434	1.1465
20°	1.1194	1.1225	1.1256	1.1287	1.1318	1.1348	1.1379	1.1410
21°	1.1139	1.1170	1.1201	1.1231	1.1262	1.1293	1.1324	1.1354
22°	1.1084	1.1115	1.1145	1.1176	1.1206	1.1237	1.1268	1.1298
23°	1.1028	1.1058	1.1089	1.1119	1.1150	1.1180	1.1211	1.1241
24°	1.0971	1.1001	1.1032	1.1062	1.1092	1.1123	1.1153	1.1184
25°	1.0913	1.0944	1.0974	1.1004	1.1035	1.1065	1.1095	1.1126

Temp.	760	762	764	766	768	770	772	774
10°	1.1976	1.2008	1.2040	1.2072	1.2104	1.2136	1.2167	1.2199
11°	1.1924	1.1956	1.1988	1.2019	1.2051	1.2083	1.2115	1.2147
12°	1.1871	1.1903	1.1934	1.1966	1.1998	1.2029	1.2061	1.2093
13°	1.1819	1.1851	1.1882	1.1914	1.1945	1.1977	1.2008	1.2040
14°	1.1766	1.1798	1.1829	1.1861	1.1892	1.1923	1.1955	1.1986
15°	1.1713	1.1744	1.1775	1.1807	1.1838	1.1869	1.1901	1.1932
16°	1.1659	1.1691	1.1722	1.1753	1.1784	1.1816	1.1847	1.1878
17°	1.1605	1.1636	1.1667	1.1699	1.1730	1.1761	1.1792	1.1823
18°	1.1551	1.1582	1.1613	1.1644	1.1675	1.1706	1.1737	1.1768
19°	1.1496	1.1527	1.1558	1.1589	1.1620	1.1650	1.1681	1.1712
20°	1.1441	1.1472	1.1502	1.1533	1.1564	1.1595	1.1626	1.1657
21°	1.1385	1.1416	1.1446	1.1477	1.1508	1.1539	1.1569	1.1600
22°	1.1329	1.1359	1.1390	1.1429	1.1451	1.1482	1.1512	1.1543
23°	1.1272	1.1302	1.1333	1.1363	1.1394	1.1424	1.1455	1.1485
24°	1.1214	1.1244	1.1275	1.1305	1.1336	1.1366	1.1396	1.1427
25°	1.1156	1.1186	1.1216	1.1247	1.1277	1.1307	1.1338	1.1368

TABLE III.

VAPOUR TENSION (AQUEOUS PRESSURE IN MILLIMETRES OF MERCURY) OF WATER AT VARIOUS TEMPERATURES.[1]

Temperature.	Pressure.	Temperature.	Pressure.	Temperature.	Pressure.	Temperature.	Pressure.
10.0°	9.140	12.8°	10.993	15.6°	13.170	18.4°	15.719
10.1	9.201	12.9	11.065	15.7	13.254	18.5	15.818
10.2	9.262	13.0	11.137	15.8	13.339	18.6	15.917
10.3	9.32	13.1	11.210	15.9	13.424	18.7	16.017
10.4	9.386	13.2	11.283	16.0	13.510	18.8	16.117
10.5	9.449	13.3	11.356	16.1	13.596	18.9	16.218
10.6	9.512	13.4	11.430	16.2	13.683	19.0	16.319
10.7	9.575	13.5	11.505	16.3	13.770	19.1	16.421
10.8	9.639	13.6	11.580	16.4	13.858	19.2	16.523
10.9	9.703	13.7	11.655	16.5	13.946	19.3	16.626
11.0	9.767	13.8	11.731	16.6	14.035	19.4	16.730
11.1	9.832	13.9	11.807	16.7	14.124	19.5	16.834
11.2	9.897	14.0	11.884	16.8	14.214	19.6	16.939
11.3	9.962	14.1	11.960	16.9	14.304	19.7	17.044
11.4	10.028	14.2	12.038	17.0	14.395	19.8	17.150
11.5	10.095	14.3	12.116	17.1	14.486	19.9	17.256
11.6	10.161	14.4	12.194	17.2	14.578	20.0	17.363
11.7	10.228	14.5	12.273	17.3	14.670	20.1	17.471
11.8	10.296	14.6	12.352	17.4	14.763	20.2	17.579
11.9	10.364	14.7	12.432	17.5	14.856	20.3	17.688
12.0	10.432	14.8	12.512	17.6	14.950	20.4	17.797
12.1	10.501	14.9	12.593	17.7	15.044	20.5	17.907
12.2	10.570	15.0	12.674	17.8	15.139	20.6	18.018
12.3	10.639	15.1	12.755	17.9	15.234	20.7	18.129
12.4	10.709	15.2	12.837	18.0	15.330	20.8	18.241
12.5	10.780	15.3	12.920	18.1	15.427	20.9	18.353
12.6	10.850	15.4	13.003	18.2	15.524	21.0	18.495
12.7	10.921	15.5	13.086	18.3	15.621		

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[1] This table is taken from Cohen's "Practical Organic Chemistry." We notice that the figures given here are uniformly less than those given in Regnault's table by, on the average, 0.0258.

TABLE IV.

Specific Gravity and Percentage of NaOH in Aqueous Solution.

Specific Gravity at 15°.	Per Cent NaOH.	Gm. NaOH in 100 c.c.	Specific Gravity at 15°.	Per Cent NaOH.	Gm. NaOH in 100 c.c.
1.007	0.61	0.6	1.220	19.58	23.9
1.014	1.20	1.2	1.231	20.59	25.3
1.022	2.00	2.1	1.241	21.42	26.6
1.029	2.71	2.8	1.252	22.64	28.3
1.036	3.35	3.5	1.263	23.67	29.9
1.045	4.00	4.2	1.274	24.81	31.6
1.052	4.64	4.9	1.285	25.80	33.2
1.060	5.29	5.6	1.297	26.83	34.8
1.067	5.87	6.3	1.308	27.80	36.4
1.075	6.55	7.0	1.320	28.83	38.1
1.083	7.31	7.9	1.332	29.93	39.9
1.091	8.00	8.7	1.345	31.22	42.0
1.100	8.68	9.5	1.357	32.47	44.1
1.108	9.42	10.4	1.370	33.69	46.2
1.116	10.06	11.2	1.384	34.96	48.3
1.125	10.97	12.3	1.397	36.25	50.6
1.134	11.84	13.4	1.410	37.47	52.8
1.142	12.64	14.4	1.424	38.80	55.3
1.152	13.55	15.6	1.438	39.99	57.5
1.162	14.37	16.7	1.453	41.41	60.2
1.171	15.13	17.7	1.468	42.83	62.9
1.180	15.91	18.8	1.483	44.38	65.8
1.190	16.77	20.0	1.498	46.15	69.1
1.200	17.67	21.2	1.514	47.60	72.1
1.210	18.58	22.5	1.530	49.02	75.0

TABLE V.

Specific Gravity and Percentage of KOH in Aqueous Solution.

Specific Gravity at 15°.	Per Cent KOH.	Gm. KOH in 100 c.c.	Specific Gravity at 15°.	Per Cent KOH.	Gm. KOH in 100 c.c.
1.007	0.9	0.9	1.252	27.0	33.8
1.014	1.7	1.7	1.263	28.0	35.3
1.022	2.6	2.6	1.274	28.9	36.8
1.029	3.5	3.6	1.285	29.8	38.5
1.037	4.5	4.6	1.297	30.7	39.8
1.045	5.6	5.8	1.308	31.8	41.6
1.052	6.4	6.7	1.320	32.7	43.2
1.060	7.4	7.8	1.332	33.7	44.9
1.067	8.2	8.8	1.345	34.9	46.9
1.075	9.2	9.9	1.357	35.9	48.7
1.083	10.1	10.9	1.370	36.9	50.6
1.091	10.9	11.9	1.383	37.8	52.2
1.100	12.0	13.2	1.397	38.9	54.3
1.108	12.9	14.3	1.410	39.9	56.3
1.116	13.8	15.3	1.424	40.9	58.2
1.125	14.8	16.7	1.438	42.1	60.5
1.134	15.7	17.8	1.453	43.4	63.1
1.142	16.5	18.8	1.468	44.6	65.5
1.152	17.6	20.3	1.483	45.8	67.9
1.162	18.6	21.6	1.498	47.1	70.6
1.171	19.5	22.8	1.514	48.3	73.1
1.180	20.5	24.2	1.530	49.4	75.6
1.190	21.4	25.5	1.546	50.6	77.9
1.200	22.4	26.9	1.563	51.9	81.1
1.210	23.3	28.2	1.580	53.2	84.0
1.220	24.2	29.5	1.597	54.5	87.0
1.231	25.1	30.9	1.615	55.9	90.2
1.241	26.1	32.4	1.634	57.5	94.0

TABLE VI.

ACETIC ACID.

Specific Gravity at 15° of Various Concentrations.				Freezing-point, as Affected by Water-content.			
Per Cent of Acetic Acid.	Specific Gravity	Per Cent of Acetic Acid.	Specific Gravity	Per Cent of Water.	Freezing-point.	Per Cent of Water.	Freezing-point.
10.0	1.014	60.0	1.069	1.0	14.8°	5.6	8.2°
20.0	1.028	70.0	1.073	2.0	13.25	6.5	7.1
30.0	1.041	80.0	1.075	2.9	11.95	8.3	5.3
40.0	1.052	90.0	1.071	3.8	10.5	9.1	4.3
50.0	1.062	100.0	1.055	4.8	9.4	9.9	3.6

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